SPECIAL COLLECTOR'S EDITION

SCIENTIFIC AMERICAN

WOMEN

Why their equality, health, wealth and safety matter to everyone

WINTER 2020

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FROM THE EDITOR

An Issue for Everyone

Women have too long been an afterthought: denied equal opportunity at home and in society and ignored by science. Recent decades brought progress toward some measure of parity in the realms of economics, politics, education and health care, but yawning gaps remain, and some are growing, threatening to undermine everyone's well-being. As the World Economic Forum put it in its 2018 report on gender disparities, "More than ever, societies cannot afford to lose out on the skills, ideas and perspectives of half of humanity to realize the promise of a more prosperous and human-centric future that well-governed innovation and technology can bring."

New research is resolving age-old and often misguided debates about the dissimilarities between the genders. Rather than inherent biological characteristics, environmental factors are coming to be seen as the driving force behind both behavioral and brain differences between men and women (*page 4* and *page 12*), though in some cases amid controversy. Gender variances certainly *do* impact the health of women: they experience higher risk for depression (*page 18*) and Alzheimer's disease (*page 24*) and are more susceptible to lesser-known versions of heart disease than men are (*page 24*).

Nowhere are women being more underserved by the biological sciences, perhaps, than in the field of reproductive medicine. Most scientists agree that a dearth of research is harming women's health (*page 26*). After more than 60 years of mass-scale reliance on birth control (which has led to crucial social outcomes for women), investigators are just now considering its physical consequences and asking if better options are possible (*page 34*).

In society and the workplace, women have long suffered the tradition of favoritism toward boys (and violence toward girls) (*page 84*) and prejudice against their abilities. Thankfully, many attitudes are evolving, and for the better—overall bias against certain groups has declined in recent years (*page 74*). Adjusting workplace policies can have a drastic effect on retaining and empowering women employees (*page 94*), such as training personnel to change perspectives that prevent the advancement of women (*page 75*) and rooting out sexual misconduct (*page 110*). Culture shifts take time, but the payoff is measurable in dollars to the economy and improvements in building the modern world.

The World Economic Forum report made note of a concerning emergence of a gender gap in AI-related skill sets, and surely all sectors of innovation cannot afford to waste the talents of women. Dollars and science aside, there is a more basic reason to care: justice and equality for all.

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IS THERE A "FEMALE" BRAIN?

The debate over whether men and women have meaningfully different brains could have profound implications for health and personal identity

By Lydia Denworth

Illustrations by Kotryna Zukauskaite

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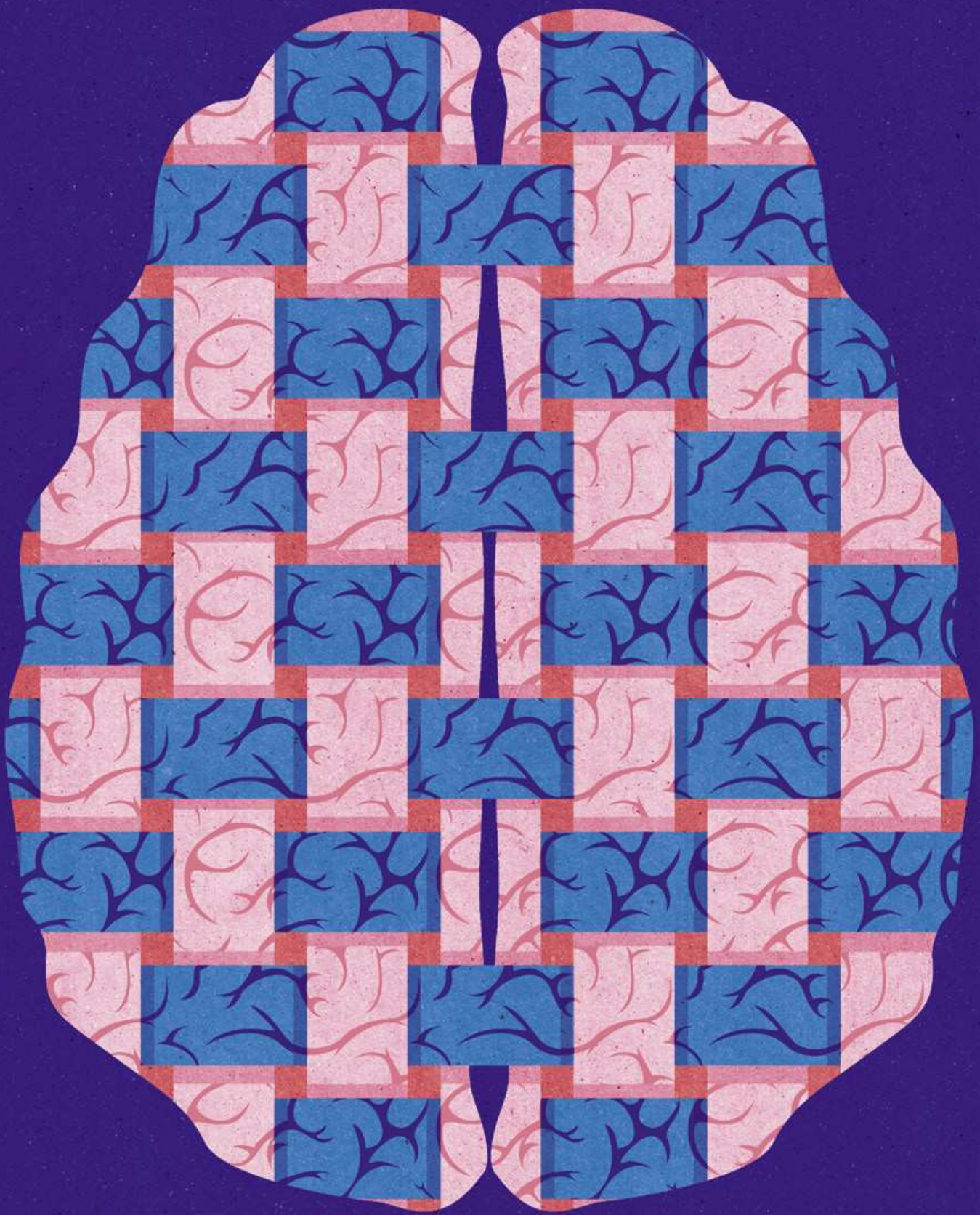

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IN 2009 DAPHNA JOEL, A NEUROSCIENTIST AT TEL AVIV UNIVERSITY, DECIDED TO teach a course on the psychology of gender. As a feminist, she had long been interested in questions of sex and gender, but as a scientist, her research had been mostly on the neural underpinnings of obsessive-compulsive behavior. To prepare for the class, Joel spent a year reviewing much of the extensive and polarized literature on sex differences in the brain. The hundreds of papers covered everything from variations in the size of specific anatomical structures in rats to the possible roots of male aggression and female empathy in humans. At the outset, Joel shared a popularly held assumption: just as sex differences nearly always produce two different reproductive systems, they would also produce two different forms of brains—one female, the other male.

IN BRIEF

A popularly held assumption asserts that male and female brains are markedly different.
Controversial new research, however, suggests that most brains are a mosaic of male and female characteristics.
Ensuing debate has roiled neuroscience and raised questions about ways in which sex and gender are considered outside the laboratory.

As she continued reading, Joel came across a paper contradicting that idea. The study, published in 2001 by Tracey Shors and her colleagues at Rutgers University, concerned a detail of the rat brain: tiny protrusions on brain cells, called dendritic spines, that regulate transmission of electrical signals. The researchers showed that when estrogen levels were elevated, female rats had more dendritic spines than males did. Shors also found that when male and female rats were subjected to the acutely stressful event of having their tail shocked, their brain responded in opposite ways: males grew more spines; females ended up with fewer.

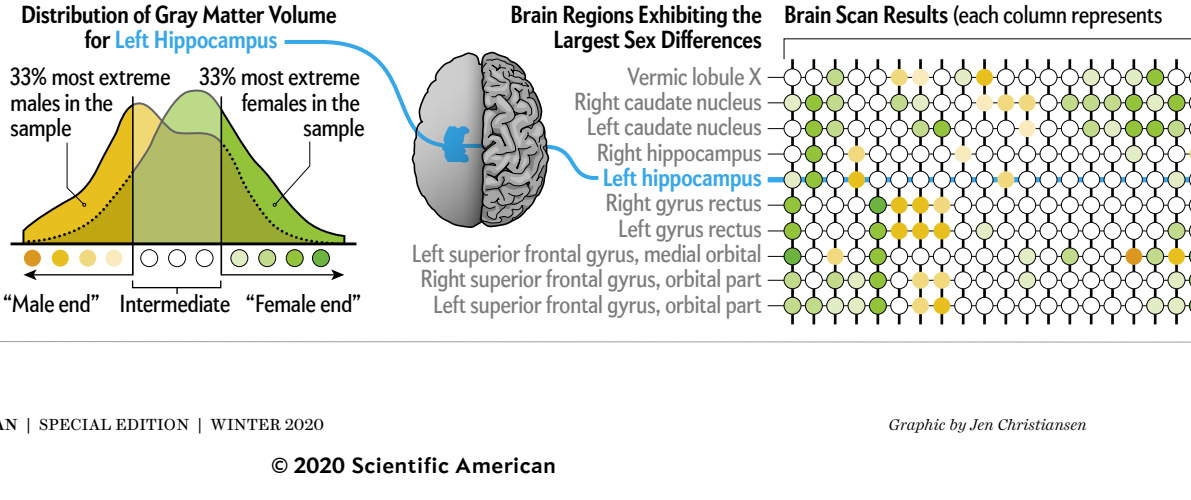
From this unexpected finding, Joel developed a hypothesis about sex differences in the brain that has stirred up new controversy in a field already steeped in it. Instead of contemplating brain areas that differ between females and males, she suggested that we should consider our brain as a "mosaic" (repurposing a term that had been used by others), arranged from an assortment of variable, sometimes changeable, masculine and feminine features. That variability itself and the behavioral overlap between the sexes—aggressive females and empathetic males and even men and women who display both traits—suggest that brains cannot be lumped into one of two distinct, or dimorphic, categories. That three-pound mass lodged underneath the skull is neither male nor female, Joel says. With her colleagues at Tel Aviv, the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig, Germany, and the University of Zurich, Joel tested her idea by analyzing MRI brain scans of more than 1,400 brains and demonstrated that most of them did indeed contain both masculine and feminine characteristics. "We all belong to a single, highly heterogeneous population," she says.

When Joel's work was published in 2015 in the *Pro-*

SOURCE: "SEX BEYOND THE GENITALIA: THE HUMAN BRAIN MOSAIC," BY DAPHNA JOEL ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 112, NO. 50; DECEMBER 15, 2015

The Mosaic Brain

Sex differences found in the human brain have led to the perception that brains are either male or female. A study by Daphna Joel of Tel Aviv University and her colleagues tells a different story. Joel's research found that the typical brain is a "mosaic," combining some features more common in males and some that appear more frequently in females, pointing to the conclusion that human brains do not belong to two distinct types categorized by sex.


Distribution of Gray Matter Volume for Left Hippocampus
33% most extreme males in the sample
33% most extreme females in the sample
"Male end"
Intermediate
"Female end"
Brain Regions Exhibiting the Largest Sex Differences
Brain Scan Results (each column represents
Vermic lobule X
Right caudate nucleus
Left caudate nucleus
Right hippocampus
Left hippocampus
Right gyrus rectus
Left gyrus rectus
Left superior frontal gyrus, medial orbital
Right superior frontal gyrus, orbital part
Left superior frontal gyrus, orbital part

Graphic by Jen Christiansen

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ceedings of the National Academy of Sciences USA, like-minded scientists hailed it as a breakthrough. "The result is a major challenge to the entrenched misconceptions," wrote Gina Rippon, a professor of cognitive neuroimaging at Aston University in England. "My hope is it will be a game-changer for the 21st century."

Longtime sex-difference researchers, meanwhile, disagreed strenuously, taking issue with Joel's methodology and conclusions, as well as her overt feminism. "The paper is ideology masquerading as science," says neurobiologist Larry Cahill of the University of California, Irvine, who argues that Joel's statistical methods were "rigged" (albeit not necessarily consciously) to favor her hypothesis. Other criticisms were more measured. "There's variability within individuals, and she shows that beautifully, but that doesn't mean there are no regions of the brain that, on average, are going to be different in men versus women," says neuroscientist Margaret M. McCarthy of the University of Maryland School of Medicine, who studies sex differences in rats.

Joel, for her part, agrees that genetics, hormones and environment do create sex differences in the brain. She even agrees that given enough information about specific features in any one brain, it is possible to guess, with a high degree of accuracy, whether that brain belongs to a female or a male. But what you cannot do, she points out, is the reverse: look at any one man or woman and predict the topography and molecular landscape of that individual's brain or personality just because you know the person's sex.

Controversial as her study is, the essence of what Joel is saying is true, says Catherine Dulac, a molecular biologist at Harvard University whose work in mice echoes Joel's findings: "There is huge heterogeneity between individuals." Acknowledging that fact has opened a new thread in the conversation about what it means to be male or female. For neuroscientists, it is no longer enough to ferret out sex differences in the brain. The debate now centers on the source, size and significance of those differences. It could have major implications for how sex and gender are considered inside and outside the laboratory—and it may have consequences as well for whether drug regimens and treatment protocols should be specialized for women and men. "Our entire society is built on the assumption that our genitals divide us into two groups not just in terms of reproduction ability or possibility but also in terms of our brain or behavioral or psychological characteristics," Joel says. "People assume the differences add up. That if you are feminine in one characteristic, you will be feminine in other characteristics. But it's not true. Most humans have a gender mosaic."

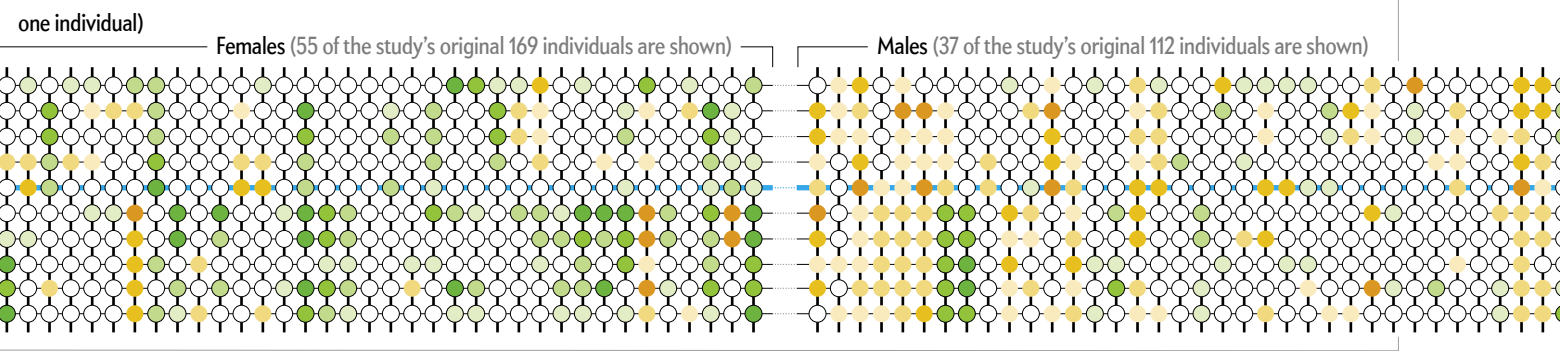
CLAIMS AND COUNTERCLAIMS

IN THE LATE 1800S, long before MRI was a gleam in any scientist's eye, the primary measurable difference in male and female brains was their weight (assessed postmortem, naturally). Because women's brains were, on average, five ounces lighter than men's, scientists declared that women must be less intelligent. As journalist Angela Saini recounts in *Inferior: How Science Got Women Wrong—and the New Research That's Rewriting the Story,* women's-rights advocate Helen Hamilton Gardener (a pseudonym) took on the experts of the day, arguing that the ratio of brain weight to body weight, or brain size to body size, had to be more relevant to intelligence than brain weight alone or "an elephant might out-think any of us." Fittingly, Gardener left her own brain to science. It was found to be five ounces lighter than the average male brain, but it was the same weight as that of the eminent male scientist who had founded the brain collection at Cornell University where her brain was stored. (For the record, Gardener was on to something. "Once you correct for brain size, most of these sex differences disappear, or they become very small," says Lise Eliot, a neuroscientist at the Chicago Medical School at Rosalind Franklin University of Medicine and Science.)

For much of the next century concrete sex differences in the brain were the province not of neuroscientists but endocrinologists, who studied sex hormones and mating behavior. Sex determination is a complex process that begins when a combination of genes on the X and Y chromosomes act in utero, flipping the

NEURAL SIGNATURES OF THE SEXES

In her 2015 study, Joel examined MRIs of more than 1,400 brains and found significant overlap among the areas of neural tissue (gray matter) showing the largest differences between males and females. In brain scans of the left hippocampus, most females and males had a volume of gray matter toward the middle on a continuum of "maleness" or "femaleness" (*graph at left and white dots from a subset of the study data below*). In addition, about a third of individuals had features at both the maleness and femaleness extremes, shown below as green (femaleness) and orange (maleness) in dots of varying shades. Only 2.4 percent, meanwhile, had just features from one extreme. The trend was also reflected in the other data sets used by the researchers, and the findings were corroborated by a subsequent analysis of personality traits, attitudes and behaviors.


one individual)
Females (55 of the study's original 169 individuals are shown)
Males (37 of the study's original 112 individuals are shown)

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switch on feminization or masculinization. But beyond reproduction and distinguishing boy versus girl, reports persisted of psychological and cognitive sex differences. Between the 1960s and early 1980s the late Stanford University psychologist Eleanor Maccoby found fewer differences than assumed: girls had stronger verbal abilities than boys, whereas boys did better on spatial and mathematical tests. Predictably, critiques followed. Janet Hyde, a psychologist at the University of Wisconsin–Madison, has conducted meta-analyses, combining the results of previous studies, and found, as she wrote in a 2016 study, that females perform as well as males in math and that "males and females are quite similar on most—but not all—psychological variables." Based on these results, Hyde developed what she calls the gender similarities hypothesis, which posits that the psychological makeup of men and women is more alike than different.

Once technology made it possible to peer inside a living brain, a long list of sex differences appeared that had nothing to do with mating or parenting. Writing in 2006 in *Nature Reviews Neuroscience,* Cahill described "a surge of findings from animals and humans concerning sex influences on many areas of brain and behaviour, including emotion, memory, vision, hearing, processing faces, pain perception, navigation, neurotransmitter levels, stress hormone action on the brain and disease states." In rats, McCarthy measures everything from the size of the collections of neurons that make up cell nuclei to the number of astrocytes and microglia, cells that form a support system for neurons. "There's irrefutable evidence of a biological basis for sex differences in the brain beginning from animals all the way up to humans," she says. But McCarthy also emphasizes that the source of sex differences in humans is more complicated than in animals that do not contend with gender, the psychological and social attributes of sex. "In humans, the fact that you're raised as a particular gender from the instant that you're born of itself exerts a biological impact on your brain," she says. In her 2009 book *Pink Brain, Blue Brain,* Eliot agrees, arguing that plasticity, the way the brain changes in response to experience, drives sex differences in behavior more than hardwired biology does.

Making the leap from brain to behavior provokes the most strident disagreements. One recent high-profile study accused of playing to stereotypes (and labeled "neurosexist") was a 2014 paper by Ruben Gur, Raquel Gur and Ragini Verma, all at the University of Pennsylvania. The group used diffusion tensor imaging, a technique showing the strength of connections among neurons, to look at nearly 1,000 brains of subjects between the ages of eight and 22. It found that males had stronger connections within the left and right hemispheres of the brain and that females had more robust links between hemispheres. The researchers concluded that "the results suggest that male brains are structured to facilitate connectivity between perception and coordinated action, whereas female brains are designed to facilitate communication between analytical and intuitive processing modes." (Counterclaim: the study did not correct for brain size.)

IN SEARCH OF VARIABILITY

INTO THIS MAELSTROM stepped Joel. Many previous studies have identified differences in single brain features and then used those differences to make claims about entire populations—the averages for women and men. Joel and her colleagues did the opposite: they used a picture of the population-level differences encountered across an entire group to ask what claims can be made about individual brains. "These are two different descriptions of the world," Joel says. Both show the same group-level differences. The critical question is: Which better describes human brains—the first, in which one type of brain is typical of males and another of females, or the second, in which most people's brains are mosaics of male and female characteristics?

Specifically, Joel's 2015 study asked two questions: How much overlap is there in features that show differences between females and males? And are brains "internally consistent"? The latter is a measure Joel developed to determine if all features in any one brain were masculine or feminine. Using four large sets of MRI data, her team identified, in each data set, several features with the greatest difference between males and females, such as the collective volume of the nerve cells' central bodies and dendritic extensions (gray matter) and their connecting fibers (white matter). They found a continuum of features. Definitive feminized and masculinized features occupied the extremes, and an intermediate zone exhibited a mix of attributes.

The researchers then assessed every brain in the data sets region by region and coded each feature [*see box on preceding pages*]. They reasoned that if brains are internally consistent, elements that show sex differences should reliably take on male or female forms. It followed that few brains should exist with both feminine and masculine traits. But between 23 to 53 percent of brains (depending on the data set) contained features from both ends of the spectrum. Brains that were internally consistent were rare—from 0 to 8 percent of those examined.

Joel cites arguments for the desirability of single-sex classrooms as a real-world example of why variability matters. "[Single-sex education] assumes that boys have one set of characteristics—for example, they are more active and have less patience—and girls have another set of characteristics. Therefore, we should separate them and treat each group differently. What we are showing is that although this is true at the group level, it's not true at the individual level. You can't divide students into a group that is very active, likes sports, is very good at mathematics, and doesn't like poetry and another group

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that is the mirror image. There are very few kids like this."

Most scientists find Joel's work demonstrating variability convincing. "Daphna's contribution was to show, individual by individual, the variability within gender," Eliot says. "Nobody ever publishes [those] data." But many find the measurement of internal consistency problematic. One response to Joel's *PNAS* paper was from Marco Del Giudice of the University of New Mexico and his colleagues. They argued that the definition Joel and her colleagues used for internal consistency was so extreme as to be biologically implausible, if not impossible. To prove it, they reran Joel's analysis using entirely different sets of biological variables—for example, comparing variability among facial features of three very different-looking monkey species. If Joel's method were valid, Del Giudice reasoned, the monkeys should show clear ("internally consistent") facial distinctions across species.

Despite notably varied appearances among the three species, the distinguishing facial features of any one monkey rarely resulted in internal consistency, as defined by Joel—hence, Cahill's view that the study is "rigged." In response, Joel and her colleagues used different analytical techniques in a 2018 study. Measuring similarity and difference mathematically rather than biologically in 2,176 human brains, they found that brains from females were almost as likely to be classified as "male" as brains from males are and that a male and a female are almost as likely to have the same brain types as two females or two males are.

The debate comes down to which matters more: the average or the individuals within the population under study. The answer often depends on the question being asked. But researchers can and do look at the same evidence and draw different conclusions. "The human brain may be a mosaic, but it is one with predictable patterns," wrote Avram Holmes of Yale University and his colleagues in response to Joel in 2015, and they believe those patterns demand statistical consideration. Biologist Anne Fausto-Sterling, a professor emerita of biology and gender development at Brown University and a critic of sex-difference research, has another perspective. "Talking about average differences is misleading if that's all we do," she says. "The brain is not a uniform entity that behaves as something male or something female, and it doesn't behave the same way in all contexts. Daphna is trying to get at the complexities of what brains actually do and how they function."

The implications of this controversy for science, especially clinical research aimed at treating disease, are considerable. Between 1997 and 2000, 10 drugs were withdrawn from the U.S. market because they carried side effects that were dangerous, even fatal. Eight of the 10 had greater health risks for women than for men. In 2013 the U.S. Food and Drug Administration reduced by half the prescription dosage of zolpidem, the generic name for Ambien, for women. After registering patients' complaints about drowsy morning commutes, researchers had discovered that the drug was still present in some women's bodies on waking. Here, too, counterclaims appear. Eliot and Sarah Richardson, a historian of science and gender at Harvard, suggest that much of the differences in zolpidem's side effects could be accounted for by body weight disparities. Weight is not the whole story, because women's higher body fat levels cause some drugs to metabolize more slowly, but precision in identifying the truly critical variables for drug dosing should be possible.

Partly in response to such concerns, starting in January 2016, the National Institutes of Health required that all preclinical research, the phase before testing in humans, must include female animals. Janine Clayton, director of the NIH Office of Research on Women's Health, was careful to say, in explaining the new policy, that including both sexes in studies does not necessarily mean looking for sex differences. Many regard this directive as an important step. McCarthy points out that various neurological diseases or disorders with an early onset, such as attention deficit hyperactivity disorder and autism spectrum disorder, are more common in males, whereas those that appear later, such as depression and anxiety, are more common in females. "In the face of that, we are compelled to look at the brain as a biological organ that differs in males and females," she says. "To not do it would be a travesty." But Joel, Fausto-Sterling and others worry that the pendulum will swing too far. They argue for research that includes sex as a variable, with an even number of male and female subjects, but that recognizes in analyzing results that "male" and "female" categories may reflect variables that have nothing to do with sex.

More broadly, if this work is to change the way society thinks about sex and gender, it might begin with terminology. "It's time to dump the word 'dimorphism,'" Eliot says. "A dimorphic structure is an ovary versus a testis. A 2 percent difference in gray matter to white matter ratio is not dimorphic. It's just a sex-related variance."

Dulac argues that we need "a more refined way to define these differences." In mice, she has found that neural circuits governing male mating behavior are also found in females, whereas maternal behavior circuits can be found in males. "It would be wrong to conclude from our work that there are no differences between males and females," Dulac says. "But the very interesting question is: How are these differences emerging, and how subtle or significant are they?"

McCarthy and Joel joined forces in 2017 to lay out a more sophisticated framework for defining what is being measured in sex-difference research and what it means. They suggest four possible dimensions: whether a trait is persistent or transient; whether it depends on context; whether it takes only one of two forms—and is thus truly dimorphic—or else falls on a spectrum; and whether it is a direct or indirect consequence of sex. This way of describing the world of sex differences is not nearly as catchy as the long-standing Mars versus Venus metaphor, but it is probably much more accurate. As a rule, complexity more closely reflects who people really are. "My mother is very nurturing, but she's a lot better at spatial navigation than my father," Eliot says. "That's a mosaic, right?" SA

Lydia Denworth is a Brooklyn, N.Y.–based science writer and a contributing editor for *Scientific American*. She is author of *Friendship: The Evolution, Biology, and Extraordinary Power of Life's Fundamental Bond* (W. W. Norton, 2020).

MORE TO EXPLORE

Sex beyond the Genitalia: The Human Brain Mosaic. Daphna Joel et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 112, No. 50, pages 15,468–15,473; December 15, 2015.

Incorporating Sex as a Biological Variable in Neuropsychiatric Research: Where Are We Now and Where Should We Be? Daphna Joel and Margaret M. McCarthy in *Neuropsychopharmacology*, Vol. 42, No. 2, pages 379–385; January 2017.

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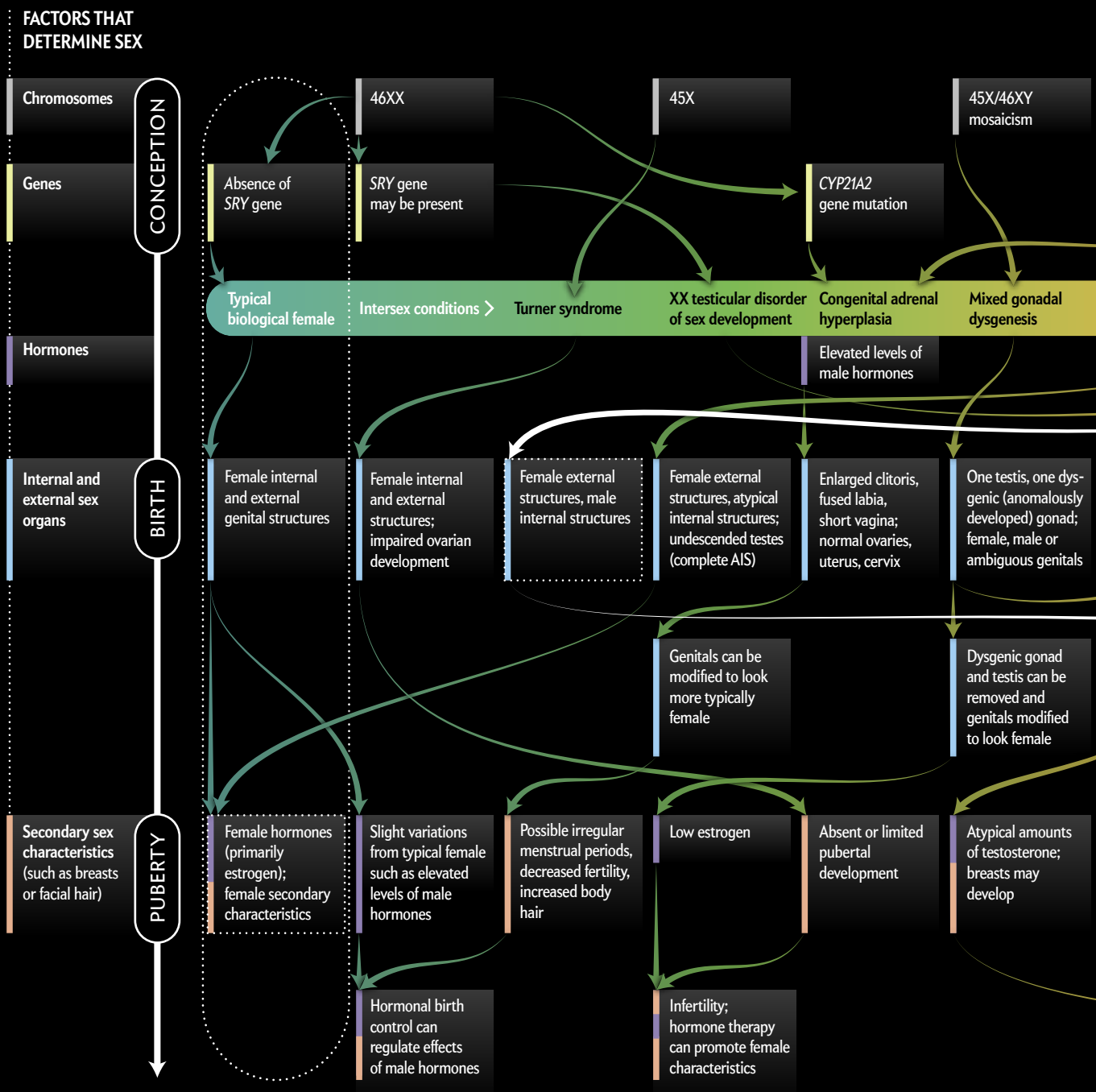
BEYOND XX AND XY

A host of factors figure into whether someone is female, male or somewhere in between

By Amanda Montañez

Humans are socially conditioned to view sex and gender as binary attributes. From the moment we are born—or even before—we are definitively labeled "boy" or "girl." Yet science points to a much more ambiguous reality. Determination of biological sex is staggeringly complex, involving not only anatomy but an intricate choreography of genetic and chemical factors that unfolds over time. Intersex individuals—those for whom sexual development follows an atypical trajectory—are characterized by a diverse range of conditions, such as 5-alpha reductase deficiency (*circled*). A small cross section of these conditions and the pathways they follow is shown here. In an additional layer of complexity, the gender with which a person identifies does not always align with the sex they* are assigned at birth, and they may not be wholly male or female. The more we learn about sex and gender, the more these attributes appear to exist on a spectrum.

**The English language has long struggled with the lack of a widely recognized nongendered third-person singular pronoun. A singular form of "they" has grown in widespread acceptance, and many people who do not identify with a binary gender use it.*


FACTORS THAT DETERMINE SEX
Chromosomes
Genes
CONCEPTION
46XX
45X
45X/46XY mosaicism
Absence of SRY gene
SRY gene may be present
CYP21A2 gene mutation
Typical biological female
Intersex conditions
Turner syndrome
XX testicular disorder of sex development
Congenital adrenal hyperplasia
Mixed gonadal dysgenesis
Hormones
Elevated levels of male hormones
Internal and external sex organs
BIRTH
Female internal and external genital structures
Female internal and external structures; impaired ovarian development
Female external structures, male internal structures
Female external structures, atypical internal structures; undescended testes (complete AIS)
Enlarged clitoris, fused labia, short vagina; normal ovaries, uterus, cervix
One testis, one dysgenic (anomalously developed) gonad; female, male or ambiguous genitals
Genitals can be modified to look more typically female
Dysgenic gonad and testis can be removed and genitals modified to look female
Secondary sex characteristics (such as breasts or facial hair)
PUBERTY
Female hormones (primarily estrogen); female secondary characteristics
Slight variations from typical female such as elevated levels of male hormones
Possible irregular menstrual periods, decreased fertility, increased body hair
Low estrogen
Absent or limited pubertal development
Atypical amounts of testosterone; breasts may develop
Hormonal birth control can regulate effects of male hormones
Infertility; hormone therapy can promote female characteristics

Graphic by Pitch Interactive and Amanda Montañez

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The Gender Spectrum

A transgender woman is a person who was assigned male at birth based on her anatomy but who identifies as a woman.

A cisgender woman is a person who was assigned female at birth based on her anatomy and who also identifies as a woman.

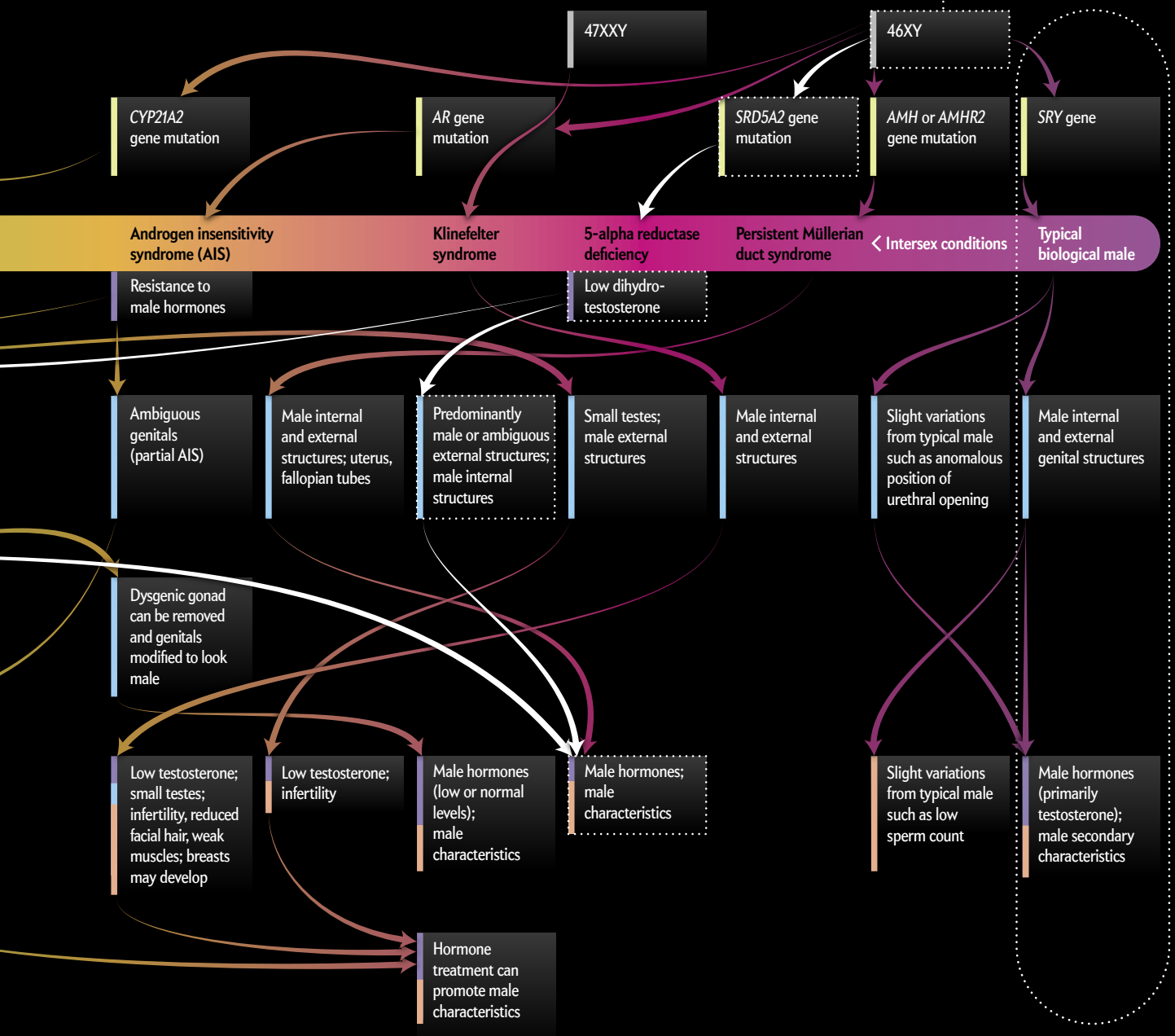
A nonbinary person is someone who identifies as neither completely female nor completely male. Such an individual may identify with both genders or neither gender, or they may be gender fluid, meaning their gender fluctuates between female and male.

A transgender man is a person who was assigned female at birth based on his anatomy but who identifies as a man.

A cisgender man is a person who was assigned male at birth based on his anatomy and who also identifies as a man.

Sexuality refers to an individual's sexual orientation or to the kind of person to whom they are attracted. Sexuality is also a spectrum but is separate from both sex and gender.

5-alpha reductase deficiency is an intersex condition that can follow multiple pathways throughout development. Affected individuals have a chromosomal makeup of 46XY, like a typical biological male, but a genetic mutation causes a deficiency of the hormone dihydrotestosterone. Patients' external anatomy can vary, so an individual might be assigned to either sex at birth, but at puberty a surge of testosterone promotes male characteristics. As a result, patients who are raised as girls often end up identifying as male.


47XXY
46XY
CYP21A2 gene mutation
AR gene mutation
SRD5A2 gene mutation
AMH or AMHR2 gene mutation
SRY gene
Androgen insensitivity syndrome (AIS)
Klinefelter syndrome
5-alpha reductase deficiency
Persistent Müllerian duct syndrome
Intersex conditions
Typical biological male
Resistance to male hormones
Low dihydro-testosterone
Ambiguous genitals (partial AIS)
Male internal and external structures; uterus, fallopian tubes
Predominantly male or ambiguous external structures; male internal structures
Small testes; male external structures
Male internal and external structures
Slight variations from typical male such as anomalous position of urethral opening
Male internal and external genital structures
Dysgenic gonad can be removed and genitals modified to look male
Low testosterone; small testes; infertility, reduced facial hair, weak muscles; breasts may develop
Low testosterone; infertility
Male hormones (low or normal levels); male characteristics
Male hormones; male characteristics
Slight variations from typical male such as low sperm count
Male hormones (primarily testosterone); male secondary characteristics
Hormone treatment can promote male characteristics

SOURCE: RESEARCH BY AMANDA HOBBS; EXPERT REVIEW BY AMY WISNIEWSKI *University of Oklahoma Health Sciences Center*

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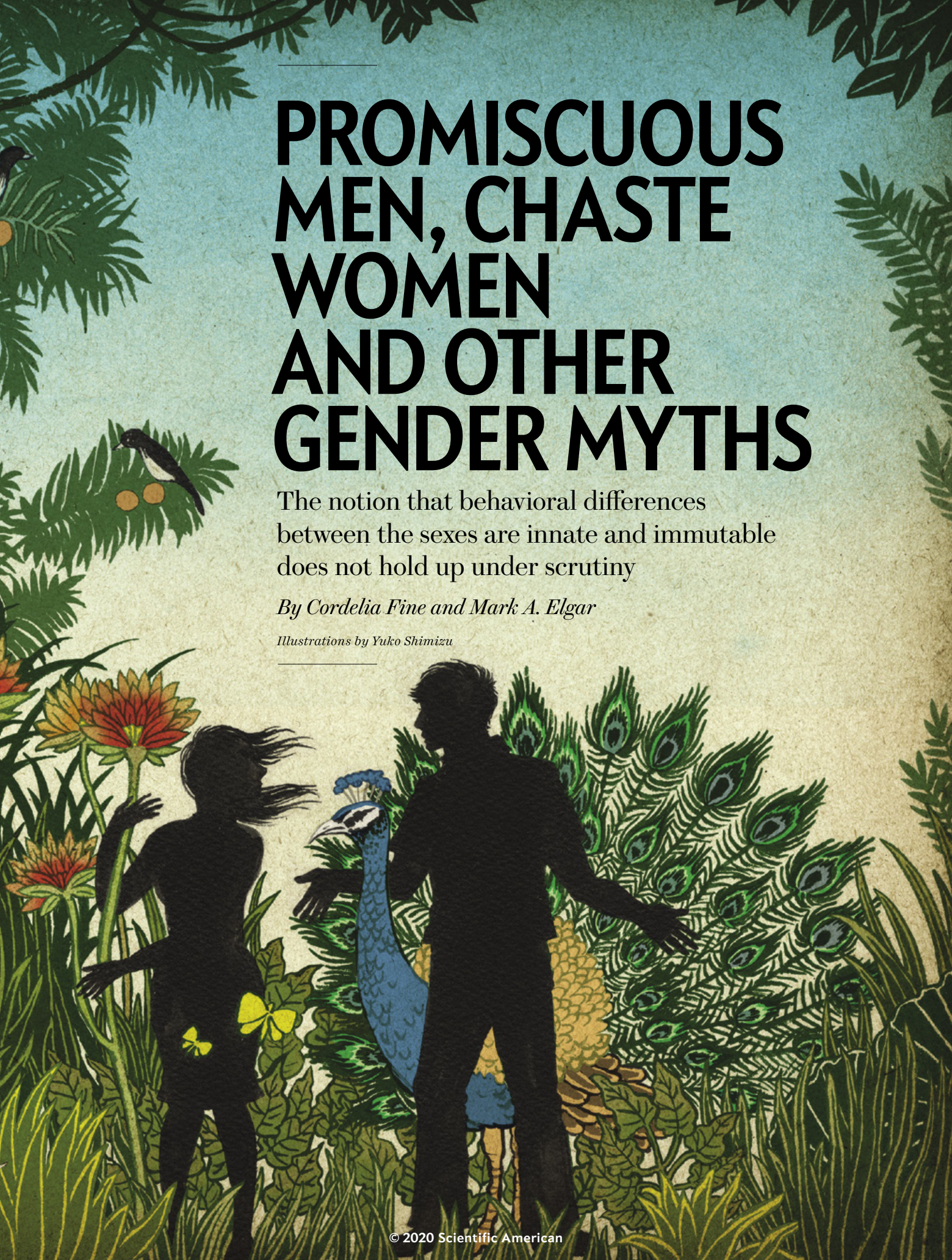
PROMISCUOUS MEN, CHASTE WOMEN AND OTHER GENDER MYTHS

The notion that behavioral differences between the sexes are innate and immutable does not hold up under scrutiny

By Cordelia Fine and Mark A. Elgar

Illustrations by Yuko Shimizu



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ONE OF AUSTRALIA'S MORE PROVOCATIVE ART MUSEUMS, the Museum of Old and New Art in Hobart, Tasmania, hosted in 2016 and 2017 an exhibition on the evolution of art. Three evolutionary scientists who guest-curated the show offered their perspectives on how evolution explains not just the characteristics of amoebas, ants and antelopes but also the uniquely human endeavor of art. One of these explanations sees art as an evolved trait akin to the peacock's effervescently colored tail, which increases its bearer's reproductive success by signaling superiority as a mate.

Hands up if this scenario conjures in your mind the image of a much feted female artist, famous for fearlessly pushing the boundaries of artistic convention, pleasurably making her way through a series of handsome young male muses? We didn't think so.

IN BRIEF

The classic evolutionary explanation of behavioral differences between men and women holds that they reflect an evolved pattern seen across the animal kingdom. Many gender gaps, in this view, are thus "natural." **But research has shown** that many of the foundational assumptions of this account are wrong. **Environmental factors,** moreover, can play a key role in the development of evolved behaviors. Progressive cultural shifts do not "go against" nature but rewrite it.

The stereotype of the daring, promiscuous male—and his counterpart, the cautious, chaste female—is deeply entrenched. Received wisdom holds that behavioral differences between men and women are hardwired, honed by natural selection over millennia to maximize their differing reproductive potentials. In this view, men, by virtue of their innate tendencies toward risk-taking and competitiveness, are destined to dominate at the highest level of every realm of human endeavor, whether it is art, politics or science.

But a closer look at the biology and behavior of humans and other creatures shows that many of the starting assumptions that have gone into this account of sex differences are wrong. For example, in many species, females benefit from being competitive or playing the field. And women and men often have similar preferences where their sex lives are concerned. It is also becoming increasingly clear that inherited environmental factors play a role in the development of adaptive behaviors; in humans, these factors include our gendered culture. All of which means that equality between the sexes might be more attainable than previously supposed.

FAST MALES, FINICKY FEMALES

THE ORIGIN of the evolutionary explanation of past and present gender inequality is Charles Darwin's theory of sexual selection. His observations as a naturalist led him to conclude that, with some exceptions, in the arena of courtship and mating, the challenge to be chosen usually falls most strongly on males. Hence, males, rather than females, have evolved characteristics such as a large size or big antlers to help beat off the competition for territory, social status and mates. Likewise, it is usually the male of the species that has evolved purely aesthetic traits that appeal to females, such as stunning plumage, an elaborate courtship song or an exquisite odor.

It was, however, British biologist Angus Bateman who, in the middle of the 20th century, developed a compelling explanation of *why* being male tends to lead to sexual competition. The goal of Bateman's research was to test an important assumption from Darwin's theory. Like natural selection, sexual selection results in some individuals being more successful than others. Therefore, if sexual selection acts more strongly on males than females, then males should have a greater range of reproductive success, from dismal failures to big winners. Females, in contrast, should be much more similar in their reproductive success. This is why being the animal equivalent of a brilliant artist, as opposed to a mediocre one, is far more beneficial for males than for females.

Bateman used fruit flies to test this idea. Although the technology for paternity testing did not exist at the time, he inferred parentage and the number of different mates of males and females as best he could. He did this rather ingeniously, by using fruit flies with different genetic mutations, including one that makes the bristles on the wings extra long, another that makes the wings curl upward, and yet another that renders the eyes very small or absent. These mutations are sometimes evident in offspring, so Bateman could estimate how many offspring each adult produced by counting the number of different mutants

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among the surviving offspring. From his data, he concluded that males were indeed more variable than females in their reproductive success (measured as offspring). Bateman also reported that only male reproductive success increased with the number of mates. This result, he argued, is why males compete and females choose: a male's reproductive success is largely limited by the number of females he can inseminate, whereas a female reaches her plateau with a single mate that provides her with all the sperm she needs.

Scholars mostly ignored Bateman's study at first. But some two decades later evolutionary biologist Robert Trivers, then at Harvard University, catapulted it into scientific fame. He expressed Bateman's idea in terms of greater female investment in reproduction—the big, fat egg versus the small, skinny sperm—and pointed out that this initial asymmetry can go well beyond the gametes to encompass gestation, feeding (including via lactation, in the case of mammals) and protecting. Thus, just as a consumer takes far more care in the selection of a car than of a disposable, cheap trinket, Trivers suggests that the higher-investing sex—usually the female—will hold out for the best possible partner with whom to mate. And here is the kicker: the lower-investing sex—typically the male—will behave in ways that, ideally, distribute cheap, abundant seed as widely as possible.

The logic is so elegant and compelling it is hardly surprising that contemporary research has identified many species to which the so-called Bateman-Trivers principles seem to apply, including species in which, unusually, it is *males* that are the higher-investing sex. For example, in some species of katydids, also known as bush crickets, the male's investment in reproduction is greater than the female's, thanks to a nutrient-rich package he provides, along with sperm, during copulation. Females thus fight one another for access to males.

The Bateman-Trivers principles also seem to provide a plausible explanation of the gender dynamics of human societies. Women are commonly understood to have less interest in casual sex with multiple partners, for instance, and to be more caring and less competitive and risk-taking. Applying the Bateman-Trivers logic, these behaviors serve to protect their investment. Contemporary advice from Facebook's chief operating officer Sheryl Sandberg to women to "lean in" at work to rise to the top thus appears to be undercut by arguments that predispositions to take risks and compete have evolved more strongly in males than in females because of greater reproductive return.

BREAKING THE RULES

BUT IT TURNS OUT that nature is not nearly so simple and neat as this line of reasoning would suggest, even for nonhuman animals. In the decades since the Bateman-Trivers principles were forged, many of their foundational assumptions have been overturned. One such change in thinking concerns the supposed cheapness of reproduction for males. Sperm is not always cheap, nor is it always abundant: for instance, male stick insects can take several weeks to recover their libido after a lengthy copulation. And more recent scrutiny of the fruit fly's reproductive habits found that males do not always take up mating opportunities. Male selectivity has consequences for females of many insects, because if they mate with a male that has copulated extensively, they risk acquiring insufficient sperm. Scarce or limited sperm is not an uncommon challenge for females, which may mate repeatedly with different males precisely to acquire enough sperm.

In fact, a reexamination of Bateman's data from the lab of Patricia Gowaty of the University of California, Los Angeles, revealed, crucially, that a female fruit fly's reproductive success also increased with her mating frequency, a pattern that has emerged for a great many other species of animals. Furthermore, field studies show that mating for females is not the given scientists once assumed it to be. In a surprisingly large number of species, a significant proportion of females do not encounter a male and are thus unable to reproduce. Nor is promiscuous mating standard practice for males. Monogyny, in which males mate only once, is not uncommon and can be an effective means of maximizing reproductive success.

Insects are not the only creatures that challenge the Bateman-Trivers principles. Even in mammals, for which investment in reproduction is particularly skewed because of the costs of gestation and lactation for females, competition is important not just for male reproductive success but also for female reproductive success. For example, the infants of higher-ranking female chimpanzees ... have higher rates of both arrival and survival than those of lower-ranking females.

In our own species, the traditional story is additionally complicated by the inefficiency of human sexual activity. Unlike many other species, in which coitus is hormonally coordinated to a greater or lesser degree to ensure that sex results in conception, humans engage in a vast amount of nonreproductive sex. This pattern has important implications. First, it means that any one act of coitus has a low probability of giving rise to a baby, a fact that should temper overoptimistic assumptions about the likely reproductive return on seed spreading. Second, it suggests that sex serves purposes beyond reproduction—strengthening relationships, for example.

Cultural and societal changes further necessitate rethinking the application of Bateman-Trivers principles to humans. The dichotomous view of the sexes that held sway in the last century has given way to one that sees differences mainly in degree rather than kind. Increased female sexual autonomy wrought by the birth-control pill and the sexual revolution has led to marked increases in premarital sex and numbers of sexual partners in women especially. And women and men report largely similar preferences for their sex lives. For example, the second British National Survey of Sexual Attitudes and Lifestyles, based on a random

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sample of more than 12,000 people between the ages of 16 and 44 surveyed around the turn of this century, found that 80 percent of men and 89 percent of women preferred monogamy.

Meanwhile the feminist movement increased women's opportunities to enter, and excel in, traditionally masculine domains. In 1920 there were just 84 women studying at the top 12 law schools that admitted women, and those female lawyers found it nearly impossible to find employment. In the 21st century women and men are graduating from law school in roughly equal numbers, and women made up about 18 percent of equity partners in 2015.

RISKS AND BENEFITS

AS WE ZOOM IN from this broad-brush perspective on gender patterns to a fine-grained examination of sex differences in behavior, the familiar evolutionary story becomes even muddier. Consider risk-taking, once assumed to be a masculine personality trait, thanks to its role in enhancing male reproductive success. It turns out that people are quite idiosyncratic in the kinds of risks they are willing to take. The skydiver is no more likely to gamble money than the person who prefers to exercise in the safety of the gym. It is largely people's perception of the potential costs and benefits of a particular risky action, not their attitude toward risk per se, that explains their willingness to take risks. These perceived costs and benefits can include not only material losses and gains but also less tangible impacts on reputation or self-concept.

This nuance is important because sometimes the balance of risks and benefits is not the same for men and women because of physical differences between the sexes or gendered norms, or both. Consider, for example, the risk of a casual sexual encounter. For a man, the gains include the near certainty of an orgasm and perhaps a burnishing of his reputation as a "stud." For a woman, sexual pleasure is far less likely from casual sex, according to a large-scale study of North American students published in 2012 by Elizabeth Armstrong of the University of Michigan and her colleagues. And thanks to the sexual double standard, her reputation is more likely to be damaged by the episode. Among young Australians, for example, sociologist Michael Flood, now at the Queensland University of Technology, found that the label "slut" retains a stronger "moral and disciplinary weight … when applied to women." Moreover, a woman bears greater physical risks, including pregnancy, sexually transmitted disease and even sexual assault.

The lens of different risks and benefits can also clarify the sexes' different propensity to assert themselves at work, as Sandberg has advised women to do. It is hard to see how a young female lawyer, looking first at the many young women at her level and then at the very few female partners and judges, can be as optimistic about the likely payoff of leaning in and making sacrifices for her career as a young male lawyer. And this is before one considers the big-picture evidence of sexism, sexual harassment and sex discrimination in traditionally masculine professions such as law and medicine.

Still, the idea that a nonsexist society could erase the psychological effects of timeless, enduring sex differences in reproductive investment seems implausible to many. An article from 2017 in the *Economist,* for example, equated the marketing-inspired tradition of the

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diamond engagement ring with the strutting peacock's extravagant tail, an evolved courtship ritual that signals a man's resources and commitment. The journalist wrote that "greater equality for women might seem to render male-courtship displays redundant. But mating preferences evolved over millennia and will not change quickly."

ENVIRONMENTAL INFLUENCE

ALTHOUGH SEX certainly influences the brain, this argument overlooks the growing recognition in evolutionary biology that offspring do not just inherit genes. They also inherit a particular social and ecological environment that can play a critical role in the expression of adaptive traits. For example, adult male moths that hailed, as larvae, from a dense population develop particularly large testes. These enhanced organs stand the moths in good stead for engaging in intense copulatory competition against the many other males in the population. One would be forgiven for assuming that these generously sized gonads are a genetically determined adaptive trait. Yet adult male moths of the same species raised as larvae in a lower-density population instead develop larger wings and antennae, which are ideal for searching for widely dispersed females.

If the development of sex-linked physical characteristics can be influenced by the social environment, it stands to reason that sex-linked behavior can be, too. One striking example comes from the previously mentioned female katydids, which compete for the males that bring them both sperm and food, in line with the Bateman-Trivers principles. Remarkably, when their environment becomes rich with nutritious pollen, their competitive "nature" wanes.

The environment is similarly important for adaptive behavior in mammals. Research published starting in the late 1970s found that rat mothers care for male and female pups differently. The males get licked more than the females in the anogenital region because the mothers are attracted to the higher level of testosterone in male pups' urine. Intriguingly, the greater stimulation from this higher-intensity licking plays a part in the development of sex differences in parts of the brain involved in basic masculine mating behavior.

As University of Sydney philosopher of science Paul Griffiths has observed, we should not be surprised that environmental factors or experiences that reliably recur every generation should be incorporated as inputs into the developmental processes that bring about evolved traits.

In our own species, these developmental inputs include the rich cultural inheritance bestowed on every human newborn. And although social constructions of gender vary across time and place, all societies weight biological sex with heavy cultural meaning. Gender socialization starts at birth, and it would only make sense if the ruthless process of natural selection were to exploit it. It may well have been adaptive in our evolutionary past for males to take these and those risks or for females to avoid them. But when culture changes—creating a very different pattern of rewards, punishments, norms and consequences, compared with those in the past—so, too, will patterns of sex differences in behavior.

Thus, the *Economist* writer was not quite right in stating that human "mating preferences evolved over millennia and will not change quickly." True, they are unlikely to change as quickly as those of katydids, with a sprinkling of pollen (although we suspect that is not what was meant). There is usually nothing simple and quick about creating cultural shifts. But change certainly can, and certainly has, taken place over timescales shorter than millennia.

Take, for example, gender gaps in the importance men and women place on a partner's financial resources, attractiveness and chastity. The very quaintness of the term "chastity" to Western ears today compared with several decades ago speaks to rapid changes in cultural gender expectations. Cross-culturally, women and men from countries with greater gender equity are more similar in all these dimensions of partner preferences than those from countries with lower equity between the sexes, according to a 2012 study by Marcel Zentner and Klaudia Mitura, both then at the University of York in England. Research has also shown that in the U.S., men now place more importance on a female partner's financial prospects, education and intelligence—and care less about her culinary and housekeeping skills—than they did several decades ago. Meanwhile the cliché of the pitiable bluestocking spinster is a historical relic: although wealthier and better-educated women were once *less* likely to marry, now they are more likely to do so.

Could we, then, see the day when the world's finest art galleries display as much art by women as by men? We certainly shouldn't let Bateman's fruit flies tell us no. SA

MY ONE AND ONLY?

Although promiscuous mating has traditionally been viewed as a male trait that evolved to maximize male reproductive success, scientists have documented dozens of species across the animal kingdom in which **females have more offspring when they mate with multiple males.**

Cordelia Fine is a professor of history and philosophy of science at the University of Melbourne. Her most recent book, *Testosterone Rex: Myths of Sex, Science, and Society* (W. W. Norton, 2017), won the 2017 Royal Society Insight Investment Science Book Prize.

Mark A. Elgar is a professor of evolutionary biology at the University of Melbourne. His research group focuses on questions about the evolutionary significance of cooperative and mating behaviors and studies the role of chemical and visual communication in facilitating those behaviors.

MORE TO EXPLORE

Sexual Selections: What We Can and Can't Learn about Sex from Animals. Marlene J. Zuk. University of *California* Press, 2002.

Rethinking Bateman's Principles: Challenging Persistent Myths of Sexually Reluctant Females and Promiscuous Males. Zuleyma Tang-Martínez in *Journal of Sex Research,* Vol. 53, Nos. 4–5, pages 532–559; 2016.

Sex-Linked Behavior: Evolution, Stability, and Variability. Cordelia Fine, John Dupré and Daphna Joel in *Trends in Cognitive Sciences,* Vol. 21, No. 9, pages 666–673; September 2017.

Testosterone Rex: Myths of Sex, Science, and Society. Cordelia Fine. W. W. Norton, 2017.

scientificamerican.com/magazine/sa

SOURCE: "RETHINKING BATEMAN'S PRINCIPLES: CHALLENGING PERSISTENT MYTHS OF SEXUALLY RELUCTANT FEMALES AND PROMISCUOUS MALES." BY ZULEYMA TANG-MARTÍNEZ, IN *JOURNAL OF SEX RESEARCH*, VOL. 53, NOS. 4–5; 2016

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NOT JUST FOR MEN

Researchers and doctors must dig deeper into gender differences before they can provide women with better treatments

By Marcia L. Stefanick

IN JANUARY 2013 THE U.S. FOOD AND DRUG ADMINISTRATION cut the recommended dose of the nation's most popular sleep drug, Ambien, in half for women but not for men. The FDA had determined that 15 percent of the 5.7 million women using zolpidem products (the active ingredient in Ambien) were experiencing driving impairment eight hours after taking the drug, compared with 3 percent of the 3.5 million male zolpidem users.

Researchers had known for a long time that women, on average, clear zolpidem from their body much more slowly than men do. Indeed, drug metabolism, tolerance, side effects and benefits differ significantly between the average man and woman for many widely prescribed medications, with women having a 50 to 70 percent higher chance of an adverse reaction. Body size, proportion of fat to muscle and a host of other factors, including hormonal influences, account for these differences. But physicians rarely consider these dynamics when writing prescriptions. Ambien, which now comes in bottles with pink (low dose) and blue (original dose) labels, is a rare example of a "sex-specific" medical recommendation.

Drug-dosing problems are just one example of how the health care system is blind to biological sex differences. As a result, women are too often treated like men. Moreover, the system can be blind to gender bias; some disorders are considered "a man's" or "a woman's," even when both sexes suffer from them. Doctors often fail to diagnose stereotypical "male" conditions in women, and vice versa, until the condition has become dangerous.

These problems arise from a serious gap in our understanding of sex differences. The vast majority of animal research has been conducted only on males, mostly on rodents. And women have been grossly underrepresented in human clinical trials. Even when both sexes are included, sex-specific analyses are generally not reported—and because most subjects are men, the findings may not pertain to women. A 2019 study found that only 7 percent of reports on adverse drug reactions in people with heart failure gave data separately for women and men. And nearly half of these showed significant differences between the two. Not surprisingly,

Illustration by Anna Parini

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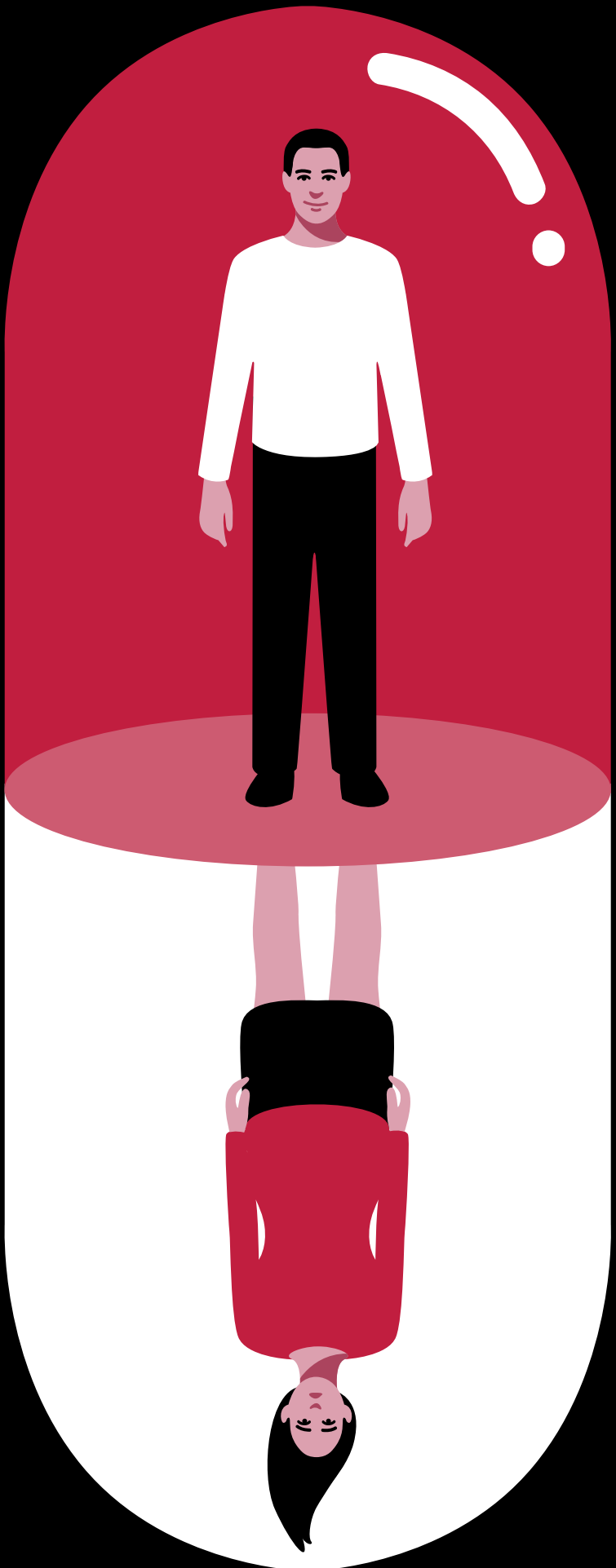

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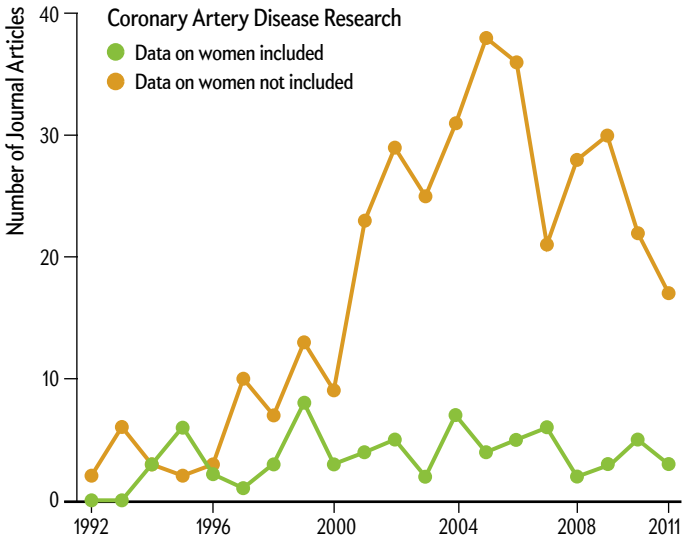
Research Bias

Medical studies often involve only male subjects or do not break out statistics for women if they are included. For example, a 2012 analysis of coronary artery disease therapies found that 355 of 427 journal articles (83 percent) either included no data for women or did not analyze data for women versus men. The paucity of research makes it difficult for doctors to assess treatments that could help women.



no one understood why a young woman hospitalized with a heart attack was twice as likely to die as a young man. Failure to include women in biomedical research was exacerbated by 1977 Food and Drug Administration guidelines that barred women of childbearing potential from participating in phase I (safety) and phase II (efficacy) trials, whether they were planning a pregnancy or not. Although the FDA now allows for inclusion of pregnant women in research that does not threaten pregnancy, few drugs are approved for pregnant women because safety and effectiveness data are not available.

FIXING THE PROBLEM

CHANGES IN PRACTICES have been long in coming. In 1990 scientists, advocates and members of Congress pushed the National Institutes of Health to establish the Office of Research on Women's Health. In 1991 the late cardiologist Bernadine Healy, the first and only woman director of the NIH, launched the Women's Health Initiative, which enrolled nearly 162,000 women across the U.S. The study led to important changes in clinical care; without it, for example, physicians might still believe they should put most older women on hormone therapy, leading to many more heart attacks and strokes and cases of breast cancer. The 1993 NIH Revitalization Act required enrollment of female (and minority) participants in federally supported phase III trials—those designed to determine how a new treatment works in a large group. The act did not, however, require enrollment of enough women to determine how a given treatment affected women specifically.

More change came in 2001, when a landmark Institute of Medicine (IOM) report emphasized the important role that "sex" played in the basic biology that underpins health care. It concluded that "every cell has a sex." Yet almost no cell biologists consider, or even know, the sex of the cells or tissues they study. Nor do they address how sex chromosomes affect the systems they are investigating. The IOM report defined sex as a biological quality or classification of sexually reproducing organisms, generally male or female, derived from chromosomes and sex hormones. Gender was defined, in human studies, as sociocultural—a person's "self-representation as male or female."

This concept can be expanded to include gender norms (social expectations of "masculine" and "feminine" behaviors) and gender relations (how people react to one another because of gender), all of which can exert powerful influences on biology. For example, men are generally stronger than women not only because of biological factors such as larger muscles but also because of gender roles: in many societies, men lift and carry most of the heavy objects. Another example might be the twofold greater incidence of (unipolar) depression in women, which may result from an interaction of biological and social factors, such as women being more likely to be sexually assaulted.

Since the IOM report, scientists, academicians and health policy advocates have been urging their institutions, journals and government agencies to confront the need to include women and female animals in research and to study sex differences. In 2009 the Gendered Innovations project at Stanford University engaged collaborators across the U.S., Canada and the European Union to develop practical methods for sex and gender analysis and to track progress on including sex and gender in research. In 2010 the Office of Research on Women's Health issued a strategic plan that identified the need to integrate sex and gender perspectives in basic science and medical research.

That same year the Canadian Institutes of Health Research went further and began asking grant applicants to indicate whether sex or gender was accounted for in their study proposals. Four years later a May 2014 notice in the journal *Nature,* written by NIH director Francis Collins and Janine Clayton, director of the Office of Research on Women's Health, unveiled policies designed to ensure that NIH-funded preclinical research consider both females and males, as well as the sex of cells. And in January 2016 the NIH began to require that sex as a biological variable be factored into research designs, analyses and reporting. If grant applicants propose to study only one sex, they must present persuasive justification for doing so. In contrast to

IN BRIEF

Doctors often assess wo en patients as if they were men because most medical research is based on male animals and men. This can lead to poor or dangerous therapies.

Physicians miss, or improperly diagnose, heart disease in women because their symptoms differ from those men typically experience. Bias is widespread in screening for mental illnesses, too.

Progress is underway, but mandates may be needed to ensure that female biology is properly, and widely, included in testing protocols, medical diagnoses and treatments.

SOURCE: "TREATMENT STRATEGIES FOR WOMEN WITH CORONARY ARTERY DISEASE: FUTURE RESEARCH NEEDS: IDENTIFICATION OF FUTURE RESEARCH NEEDS FROM COMPARATIVE EFFECTIVENESS REVIEW NO. 66." BY ROWENA J. DOLOR ET AL.; AGENCY FOR HEALTHCARE RESEARCH AND QUALITY, REPORT NO. 13-EHC073-EF; FEBRUARY 2013

Graphic by Jen Christiansen

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the Canadian Institutes, however, the NIH did not address the influence of gender on biology.

A MAN'S DISEASE

GENDER BIASES profoundly influence diagnoses and treatments and therefore health outcomes. Despite years of "Red Dress" campaigns, most people and many physicians still think of heart disease as a man's disease. They are surprised to learn that heart disease is the number-one killer of U.S. women, far exceeding deaths from breast cancer. Younger women, in particular, often go undiagnosed because physicians do not consider the possibility. Furthermore, women commonly report a range of symptoms beyond chest pain—the key complaint of men—including back pain, nausea, headache, dizziness and pain down the right arm (not just the left). Physicians often refer to these common symptoms as "atypical" because men do not report them.

In addition, although men and older women are likely to have a blockage in one or more of the coronary arteries from localized plaque—a buildup of cholesterol, fat and other substances—younger women are more likely to have diffuse plaque that lines and narrows the entire artery, resulting in inadequate blood supply to the heart. Because no specific blockage is detected, they may be diagnosed as "free of heart disease" yet at high risk of a fatal heart attack. Although newer diagnostic tests can detect this nonobstructive disease, a physician has to consider the possibility that a young woman has heart disease to order them. Prevention and treatment guidelines for women are still based predominantly on male data, despite growing evidence of sex differences in risks and treatment outcomes.

Pregnancy, now recognized as a major cardiovascular stress test, also contributes to sex disparities, yet researchers have only recently begun to realize the serious long-term consequences. Pregnancy-related hypertension and preeclampsia, as well as gestational diabetes (high blood glucose developed during pregnancy), increase a woman's chance of developing subsequent cardiovascular disease nearly twofold, as well as her risk of developing type II diabetes.

HARD TO DECIPHER

SEX DIFFERENCES and gender biases influence medical diagnoses and treatments for *everyone*. Osteoporosis, characterized by reduced bone strength, is considered a woman's disease because white women have twice the lifetime risk of fracturing a bone as white men do. Fracture prevention trials have included few men. Yet men account for nearly one in three hip fractures, and their medical outcomes are worse.

Men are more susceptible to viral, bacterial, parasitic and fungal infections than women are, although women have greater rates of sexually transmitted infections such as HIV and herpes simplex virus 2. On the other hand, the more robust immune system of women may explain why they constitute 70 percent of the 20 million Americans with autoimmune diseases, in which the immune system attacks one's own body tissues. Pregnancy may play a role here as well. Some fetal cells cross into the mother's blood and are found in her circulation decades later, and they have been implicated in some autoimmune diseases.

Sex and gender also shape neurological and mental diseases. Accumulating evidence suggests that the placenta of the male fetus responds to environmental stressors by promoting fetal growth, whereas the female placenta promotes gene and protein expressions that increase chances of survival. This difference may contribute to developmental disorders that are diagnosed more often in boys, such as autism and dyslexia—although diagnostic methods may overlook girls.

Gender bias surrounding mental illnesses seems to be widespread. The suggestion that boys and men manifest depression with anger, rather than withdrawal, may arise from a biased expectation that males externalize behaviors and females internalize them. Some mental health professionals around the world still assign certain symptoms almost exclusively to women, such as being "hysterical," whereas men are likely to be diagnosed as "antisocial." These biases affect treatments and health outcomes. In addition, a woman is much more likely to be diagnosed with depression than a man with identical presentation because of gender biases within the medical system. Women also receive more antidepressants when reporting pain because of an incorrect belief that they have a greater tolerance to it. In fact, they have a lower threshold for almost every kind of pain investigated.

Bias is rampant when it comes to the brain. Pop psychology loves the idea that men and women have different brains. Reports show that males have more cortical connections within each of the brain's two hemispheres, whereas women have more connections between the hemispheres. But the reports fail to mention that 86 to 88 percent of all these combined connections are similar—suggesting that male and female brains are more alike than different. Research also increasingly shows that any individual's brain development over a person's lifetime is greatly influenced by neuroplasticity—the ability of brain cells to rewire over time. If the daily experiences of boys and men differ markedly from those of girls and women, differences in brain structure and function should be expected.

This complicated picture makes it difficult to pin down causes and treatments for brain illnesses. Two thirds of the more than five million Americans who have Alzheimer's disease are women, not only because many more women than men survive to age 65 but also because more women acquire the disease across all age groups.

TIME TO GET PERSONAL

CLEARLY, MEDICAL RESEARCHERS and physicians have a lot of untangling to do before they can offer better health care to women. A deeper understanding of sex differences will improve health directives for men, too. In 2015 the NIH launched a Precision Medicine

LOPSIDED SCIENCE

5.5 to 1

The ratio of neuroscience studies that incorporate only male animals compared with ones that use just females. Animal research provides the underpinning for many psychoactive drugs.

SOURCE: "SEX BIAS IN NEUROSCIENCE AND BIOMEDICAL RESEARCH," BY ANNALIESE K. BEERY AND IRVING ZUCKER, IN *NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS*, VOL. 35, NO. 3; JANUARY 2011

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Note to Doctor: Women Are Not Men

Medical studies relied heavily on men or male animals in the past, which slowed progress in women's health care, according to the Institute of Medicine. Although researchers are finally improving the mix, women and female animals are still in the minority. Parity is needed because many illnesses affect women differently than men. Women often respond differently to treatments as well. Here is just a sample.

CANCER

Overall, cancer kills more men than women, but averages mask important sex differences in specific types of cancer. Recognizing disparities could prevent doctors from overlooking or misdiagnosing symptoms.

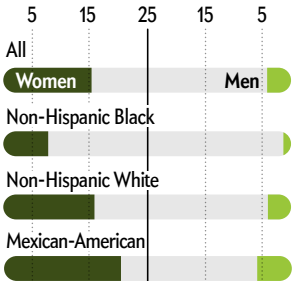
Women have a higher risk than men of developing right-sided colon cancer, a more aggressive killer than left-sided colon cancer. Diagnosis in women also tends to be more delayed.

More men than women die from lung, colon, kidney and liver cancer. But overall cancer risk is higher for women under age 50.

Being taller is a risk factor for many cancers in both men and women and may account for one third of the greater total cancer risk in men.

Side effects from fluorouracil, a common chemotherapy drug, are significantly worse in women; so are effects from many other cancer drugs.

Prevalence of Osteoporosis (percent of U.S. residents aged 50 and up, 2010)



BONES AND JOINTS

Sex and gender differences work both ways. White women are twice as likely as white men to have osteoporosis—fragile bones—but the risk of death from fragile-bone fractures is 50 percent greater for men.

Women undergo about two thirds of all knee replacements, but there is no evidence that "gender-specific" knees, marketed by manufacturers, improve outcomes. Overemphasizing sex differences can be a problem.

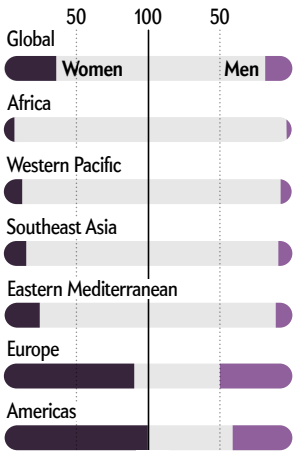
DISEASE

Certain thyroid autoimmune illnesses such as Hashimoto's disease and Graves' disease are 7 to 10 times higher in women; so is lupus.

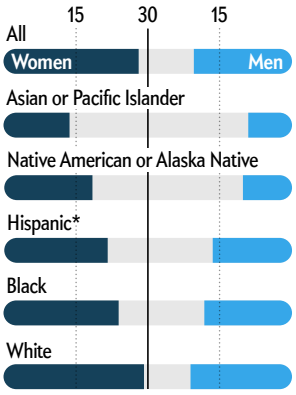
Rheumatoid arthritis, multiple sclerosis and scleroderma are at least 2 to 3 times higher in women.

More women than men are infected by herpes simplex virus 2.

Prevalence of Multiple Sclerosis (cases per 100,000 people, 2015)



Deaths from Alzheimer's Disease (age-adjusted deaths in U.S. per 100,000 people, 2014)



*Includes Hispanic black and Hispanic white

MENTAL ILLNESS

Twice as many women as men are diagnosed with anxiety or depression.

Almost two thirds of Americans with Alzheimer's disease are women. The *APOE4* gene is more strongly linked to the disease in women. X and Y chromosomes may also play a role.

The number of older U.S. women dying of Alzheimer's is now greater than all U.S. women who die of breast cancer.

Illustrations by Mesa Schumacher, Graphics by Jen Christiansen

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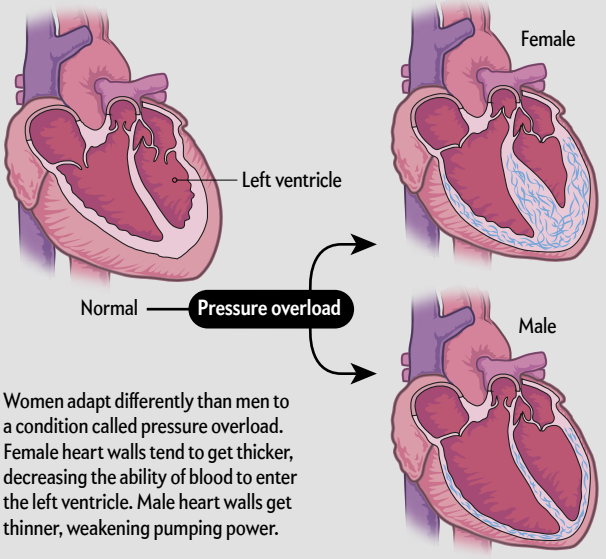
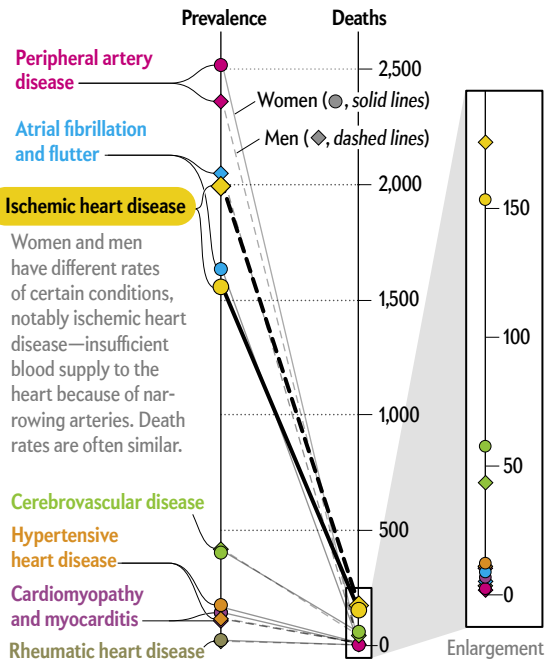
HEART PROBLEMS

Heart complications often take different forms in women and men. Heart failure in women is more likely to result from left ventricle walls that stiffen and thicken (*illustration*). Among electrical problems, an irregular heartbeat is more common in men, while rapid heartbeat is more common in women—and certain drugs can make the condition life-threatening. Heart valve diseases vary, too. Blood clotting is greater in women, which can affect treatments; that trait may have evolved to prevent excess blood loss during childbirth.



Women adapt differently than men to a condition called pressure overload. Female heart walls tend to get thicker, decreasing the ability of blood to enter the left ventricle. Male heart walls get thinner, weakening pumping power.

Cardiovascular and Circulatory Disease
(cases per 100,000 people in U.S., 2015)



Terminology for charts was taken from studies cited.

SOURCES: "THE RECENT PREVALENCE OF OSTEOPOROSIS AND LOW BONE MASS IN THE UNITED STATES BASED ON BONE MINERAL DENSITY AT THE FEMORAL NECK OR LUMBAR SPINE," BY NICOLE C. WRIGHT ET AL., IN *JOURNAL OF BONE AND MINERAL RESEARCH*, VOL. 29, NO. 11; NOVEMBER 2014 (*osteoporosis*); "GBD COMPARE." INSTITUTE FOR HEALTH METRICS AND EVALUATION, SEATTLE, WA. ACCESSED JULY 2017 *http://vizhub.healthdata.org/gbd-compare* (*multiple sclerosis and heart disease*); "DEATHS: FINAL DATA FOR 2014," BY KENNETH D. KOCHANEK ET AL., IN *NATIONAL VITAL STATISTICS REPORTS*, VOL. 65, NO. 4; JUNE 30, 2016 (*Alzheimer's disease*); "MECHANISTIC PATHWAYS OF SEX DIFFERENCES IN CARDIOVASCULAR DISEASE," BY VERA REGITZ-ZAGROSEK AND GEORGIOS KARARIGAS, IN *PHYSIOLOGICAL REVIEWS*, VOL. 97, NO. 1; JANUARY 2017 (*heart illustrations*)

Initiative to address the problem that most treatments have been designed for the "average patient" instead of each individual. "Precision" or "personalized" medicine is expected to take into account variability in genes, environment and lifestyle for each person. Yet genome-wide studies that try to pinpoint genetic variants that may be linked to specific diseases have generally excluded X and Y chromosomes, suggesting that sex is not an important focus of precision medicine.

In 2015 the Canadian Institutes of Health Research rolled out an online training course on sex and gender in health research, and the League of European Research Universities released a report on how to integrate sex and gender into research processes. In 2016 the NIH mandated that researchers consider sex as a biological variable in animal and human studies, and a panel of 13 experts representing nine countries developed the Sex and Gender Equity in Research guidelines, a comprehensive procedure for reporting sex and gender information in study design, data analyses, results and interpretation of findings. Despite two U.S. educational summits calling for integrating sex- and gender-based evidence into medicine since 2015, relatively little progress has been made. A third such summit is scheduled to take place in Philadelphia in September 2020 and will assess the progress over the past five years. Advancing understanding of sex and gender differences in health and disease and integrating those perspectives into emerging basic science fields and in translational research and technologies are two of the key themes of the recently released NIH report on women's health research.

We might need further mandates, through policy and funding restrictions, to ensure that female biology makes it into textbooks and testing protocols. We might also need to require best practices—standards of care that must be adhered to as part of the ethical code of "do no harm"—to ensure that clinicians and health care providers consider both sex and gender in medical diagnoses, screening and treatments. Both women and men would benefit enormously. Without sex and gender as a focus, physicians cannot achieve the precision medicine, specific to each one of us, that we all hope to receive. SA

Marcia L. Stefanick is a professor of medicine at the Stanford Prevention Research Center and a professor of obstetrics and gynecology at the Stanford University School of Medicine. She is also director of the Stanford Women and Sex Differences in Medicine Center and is conducting a large trial of older women related to heart disease prevention and healthy aging.

MORE TO EXPLORE

Exploring the Biological Contributions to Human Health: Does Sex Matter? Institute of Medicine. National Academies Press, 2001.

Gendered Research and Innovation: Integrating Sex and Gender Analysis into the Research Process. League of European Research Universities, September 2015.

Gendered Innovations project, Stanford University: http://genderedinnovations.stanford.edu

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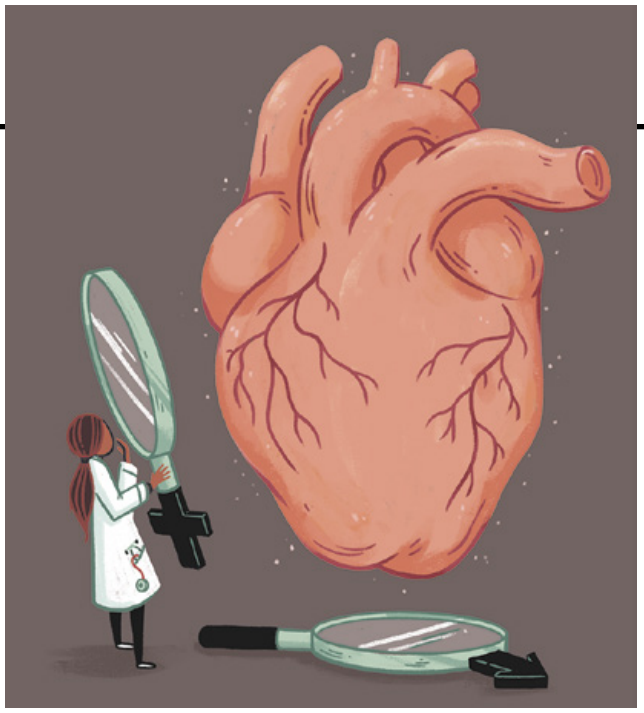
WHAT AILS A WOMAN'S HEART

The more we look, the more we find sex differences in cardiovascular disease

By Claudia Wallis



Consider almost everything you know about heart disease, particularly the garden-variety type involving high cholesterol levels, clogged coronary arteries, stents and bypass surgeries. Now I want you to rebrand all that as "male-pattern" cardiovascular disease. That's how some researchers are reframing it after taking a closer look at heart disease in women.

For years cardiologists were baffled as to why up to half of women with classic symptoms of blocked vessels—chest pain, shortness of breath and an abnormal cardiac stress test—turn out to have open arteries. Doctors called it "cardiac syndrome X." They didn't understand it, and many women were subjected to repeated angiograms in search of blockages that weren't there.

That still happens today, but more doctors now recognize that despite having open arteries, about half of women with this pattern nonetheless have ischemia—poor blood flow through the heart. The condition has gained a mouthful of a name: ischemia and no obstructive coronary artery disease, or INOCA.

Cardiologist C. Noel Bairey Merz has spent more than 20 years overseeing the Women's Ischemia Syndrome Evaluation (WISE) study, aimed at demystifying INOCA and related conditions. Although male-pattern disease is the most prevalent type in both sexes, "INOCA probably comprises 25 to 30 percent of ischemic heart disease in women and 10 percent in men," says Bairey Merz,

WHY SEX MATTERS IN ALZHEIMER'S

To fight the disease, we need to look at sex-specific risks

By Rebecca Nebel

Growing older may be inevitable, but getting Alzheimer's disease is not. Although we can't stop the aging process, which is the biggest risk factor for Alzheimer's, there are many other factors that *can* be modified to lower the risk of dementia.

Yet our ability to reduce Alzheimer's risk and devise new strategies for prevention and treatment is impeded by a lack of knowledge about how and why the disease differs between women and men. There are tantalizing hints in the literature about factors that act differently between the sexes, including hormones and specific genes, and these differences could be important avenues of research. Unfortunately, in my experience, most studies of Alzheimer's risk combine data for women and men.

For that reason, researchers at the Society for Women's Health Research Interdisciplinary Network on Alzheimer's Disease published a review paper in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* that calls for greater analysis of research data by sex to stimulate new approaches that will improve prevention, diagnosis and treatment of Alzheimer's.

We have some evidence, for example, that sex hormones such as estrogen influence the course of the disease, but we do not understand enough about why and how. Ovaries are the primary source of estrogen for premenopausal women, and surgical removal of a woman's ovaries before menopause is associated with a higher risk of dementia. But using estrogen therapy after surgery until age 50 negates that risk. This fact suggests that estrogen may be protective in premenopausal women.

In men, there are conflicting studies as to whether androgen-deprivation therapy, which is used to treat prostate cancer, increases the risk for Alzheimer's. Further investigation is needed into the role of sex hormones, the use of different hormonal treatments and the ways they each impact Alzheimer's risk.

Among risk factors that affect both women and men, some are more common in one sex. For example, depression and sleep apnea are both risk factors for dementia, but depression is twice as common in women, and sleep apnea is much more common in men. Similarly, low education and poor job attainment are Alzheimer's risk factors, but traditionally women have not had the same access to education and job opportunities as men, which puts them at increased risk.

Illustration by Celia Krampien

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director of the Barbra Streisand Women's Heart Center at Cedars-Sinai's Smidt Heart Institute. WISE data show that after diagnosis, women with the disorder face a 2.5 percent annual risk of dying, suffering a nonfatal heart attack or stroke, or being hospitalized for heart failure. They are also four times more likely than men to be readmitted to a hospital within 180 days of being treated for a heart attack or severe chest pain.

The initial mystery of INOCA was how the heart could be starving for blood if its main arteries are not blocked. The answer often lies in the smaller branches and twigs of the vascular system—arterioles and capillaries that deliver oxygen and nutrients to heart muscle. The walls of these vessels are too thin to accumulate plaque, but they can become dysfunctional, failing to contract or dilate as needed—when, for example, someone is walking up a flight of stairs or is hit by an emotional shock.

Half to two thirds of INOCA cases can be traced to such dysfunction, which is detected with specialized scanning or testing via catheter. Why women are so susceptible is not fully known, says cardiologist Puja K. Mehta of Emory University's Women's Heart Center. Many of the usual suspects are implicated—smoking, diabetes, high blood pressure, high cholesterol—but a history of problems during pregnancy, such as elevated blood pressure and diabetes, and of depression and autoimmune diseases, both of which are more common in women, may also contribute.

Optimal therapy remains a work in progress. Smallish studies show that many drugs used to treat male-pattern disease, including statins and ACE inhibitors, can help patients with INOCA. The first truly large-scale trial comparing an intensive drug regimen with "usual care" in 4,422 women got underway in early 2018. Its results, due out in 2022, should help set treatment standards.

Effective therapy is badly needed. Women with microvascular dysfunction often go on to develop heart failure—and not just any heart failure but a particularly female version. In men, the typical problem is that the ventricles don't squeeze effectively; this is called heart failure with reduced ejection fraction, or HFrEF (pronounced "hef-ref"). In women, the more frequent issue is that the ventricles don't relax enough to fill properly; this is heart failure with preserved ejection fraction, or HFpEF ("hef-pef").

Both types are rising in the U.S. because the population is getting older, heavier and more diabetic. As cardiologist Linda Peterson of the Washington University School of Medicine in St. Louis notes: "More people survive their heart attacks, so they are dying of heart failure down the road." HFrEF is well understood. "We have buckets of knowledge and treatment for [it]," Bairey Merz says, "but essentially no effective therapy for HFpEF. Had we studied women 50 years ago, we wouldn't be in this situation."

Just about everything we know about heart disease in women has been learned since the early 1990s, when the National Institutes of Health began requiring that women be included in the studies it funds. Before that, most medical research was conducted on guys: male patients, male rats, male mice, male monkeys, male cells. Like most gender gaps, this one is closing slowly. SA

Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times, Time, Fortune* and the *New Republic*. She was science editor at *Time* and managing editor of *Scientific American Mind*.

The e4 allele of the *APOE* gene is the strongest and most common genetic risk factor for Alzheimer's in both women and men, but it confers a greater risk in women. Women with *APOE* e4 are at increased risk of developing Alzheimer's, compared with women without the allele and men with and without it.

Learning how sex impacts risk factors at various times across a life span is also critical. For example, in cardiovascular disease, taking aspirin helps to reduce heart attack and stroke risk in women aged 65 years and older. This effect is not seen in younger women. It is possible that certain Alzheimer's risk factors may be strongest at certain points during our lives, and exploring this correlation is key for prevention and early intervention.

Risk factors are just one of the areas in which we need more research into the differences between the sexes in Alzheimer's. Scientists have often overlooked sex differences in diagnosis, clinical trial design, treatment outcomes and caregiving. This bias has impeded progress in detection and care.

Approaches that incorporate sex differences into research have advanced innovation in respect to many diseases. We need to do the same in Alzheimer's. Looking at these differences will greatly enhance our understanding of this thief of minds and improve health outlooks for all. SA

Rebecca Nebel was director of scientific programs at the Society for Women's Health Research, a national nonprofit organization, and is now at the National Institutes of Health.

Illustration by Cornelia Li

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THE POINT OF A PERIOD

Age-old taboos against menstruation have led to a lack of research on how women's cycles work, with serious consequences for their health

By Virginia Sole-Smith

Photographs by Jamie Chung

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IN 2007 SUSAN BROWN ENCOUNTERED THE REPELLING POWER OF PERIOD BLOOD. While studying what menstrual fluid might reveal about a woman's health, she wanted data from a cross section of subjects beyond the student volunteers at the University of Hawaii at Hilo, where she worked as an evolutionary psychologist. Brown's team members set up a booth near the entrance of a Walmart in downtown Hilo and hung a sign that said, "Menstrual Cycle Research." Then they waited. All afternoon women and men would spot the sign, then gingerly skirt past without making eye contact.

About six months later Brown and her Hilo colleague Lynn Morrison presented their findings at the annual meeting of the American Association of Physical Anthropologists. A wave of "nervous twittering" broke out when Morrison described carrying menstrual blood samples down the hallway of their laboratory to analyze hormone levels and other biomarkers. "The audience was fine discussing a woman's cycle in the abstract," Brown explains, "but not menstrual blood itself."

That aversion has influenced women's relationships to their own bodies as well as how the medical establishment manages women when things go wrong with their reproductive health. "Our menstrual taboo is at the core of how this science is getting done," Brown says of research on menstruation.

Or not getting done, as the case may be. It is hard to measure how much money is spent on period research, but experts agree the subject is underfunded. "It's a chicken-and-egg situation, where there's not much funding for research, so there's also not much quantifying of that lack of research," says Elizabeth Yuko, a bioethicist at Fordham University.

Yet period disorders are incredibly common. When Saudi Arabian researchers surveyed 738 female college students in a 2018 study, they found that 91 percent reported at least one menstrual problem: some got their periods irregularly or not at all; others reported excessive levels of bleeding and pain. Different studies show that as many as one in five women experiences menstrual cramps severe enough to limit her daily life. About one in 16 worldwide suffers from endometriosis, a disease where menstrual blood and tissue migrate outside a woman's uterus and form painful lesions in her pelvic cavity. And one in 10 women has polycystic ovarian syndrome, a hormonal imbalance that disrupts a woman's cycle and is a leading cause of infertility. "You can argue we need to put our resources toward researching the life-and-death stuff," Yuko says. "But that argument falls apart because we've had no problem funding erectile dysfunction research."

Menstruation, of course, is essential to human reproduction and therefore survival. It is also one of the biological processes that makes us special because humans, chimpanzees, bats and elephant shrews are among the only animals on earth that go through it. The vast majority of mammals signal fertility through estrus, the period when females are ovulating and display their sexual receptivity via genital swelling, behavioral changes or pronounced alterations in body odor. The female human body, however, conceals this critical window. Instead our most visible sign of potential fertility is menstrual blood, which, ironically, appears after the fertile period has closed. The endometrial lining of the uterus thickens over the course of a woman's cycle as her estrogen level rises. If none of the eggs she releases at ovulation joins with a sperm and implants in that lining as a fertilized zygote, then levels of estrogen and another hormone called progesterone drop, triggering the uterus to shed the thickened endometrium so it can start fresh in the next cycle.

But beyond this basic picture, scientists are still struggling to understand fairly fundamental questions: Why do we share this process with at least six species of bats, for example, but not monkeys? And just what is menstrual blood, exactly? "It's quite different from regular blood," Brown notes. "We know it can't clot and is full of immune agents, but we don't know much about what they do." It is also unclear why we shed this biological tissue so dramatically when most mammals that experience estrus appear

IN BRIEF

Squeamishness about female menstruation has led to limited research on how periods work and why they evolved.

Yet many women experience serious pain and other problems with their periods, and medicine has few treatments.

Scientists are just beginning to grapple with questions such as whether it is healthy to have many periods throughout a lifetime and whether suppressing menstruation through birth control is beneficial.

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to reabsorb their endometrial linings at the end of each cycle. Even less is known about why so many women—up to 80 percent by some estimates—experience cramps, bloating, fatigue, anger or other symptoms just before the onset of menstruation. "We know so little about menstruation," says Tomi-Ann Roberts, president of the Society for Menstrual Cycle Research and a professor of psychology at Colorado College, and what scientists do know is often badly communicated with the public. "Because of this, our attitudes toward menstruation are overwhelmingly negative. This has real consequences for how we can begin to understand healthy menstruation, as well as menstruation-related disorders and the treatment options available."

MENSTRUAL CUPS can be a reusable, environmentally friendly alternative to tampons and pads.

MASKING MENSTRUATION

THE TABOO has taken many forms. In 1920 a Hungarian-born pediatrician working in Vienna named Béla Schick published a collection of anecdotal observations: When he asked a menstruating woman to handle flowers, they wilted within minutes. When he compared the bread dough made by several women, the loaf made by the one having her period rose 22 percent less. Schick concluded that menstrual blood contained a kind of poison. By the early 1950s Harvard University scientists were referring to "menotoxins" and injecting menstrual blood into animals to observe the effects. Some of those animals died, most likely because the blood samples carried bacteria and other contaminants. Not much came of these experiments in terms of useful data, but the notion that menstrual blood contains mysterious and even dangerous properties has persisted in the scientific literature and our cultural imagination.

By the late 1950s research around menstruation had shifted to center almost entirely on preventing unplanned pregnancies at a time when maternal and infant mortality was troublingly high, especially in poor communities. In 1923 Margaret Sanger, the activist, nurse and founder of the organizations that would later become Planned Parenthood, wrote that "Birth Control means liberation for women and for men." In 1951 she met a physiologist named Gregory Pincus, who had performed what was considered at the time to be the first in vitro fertilization of rabbits. With Sanger securing funding, Pincus set up a lab to test formulations of synthetic versions of hormones that regulate the menstrual cycle and teamed up with John Rock, a Boston obstetrician-gynecologist, to run clinical trials of the drug.

After a study of almost 60 women in and around Boston, Pincus and Rock turned to Puerto Rico to run the first large-scale trial of the drug that the U.S. Food and Drug Administration would approve in 1960 as the first oral contraceptive. They recruited 265 Puerto Rican women, many of them poor, to the study without the level of "informed consent" required today. Twenty-two percent of the participants dropped out after reporting side effects such as nausea, dizziness, headaches and vomiting. The study's medical director argued that the pill "caused too many side reactions to be generally acceptable." Nevertheless, it went to market.

The pill was, of course, celebrated as a huge breakthrough. "It was the first form of birth control separate from sex that women could completely control," notes Elizabeth Kissling, a professor of women and gender studies at Eastern Washington University. It is impossible to overstate the freedom the pill represented for women, whose reproductive lives were otherwise largely under male control. But liberation came with a price. By the late 1960s patients across the U.S. were reporting the same symptoms documented during the Puerto Rican trial. Despite many reformulations over the ensuing decades, side effects remain a problem for many women on the pill; risks for breast cancer, blood clots and stroke may also be higher. In their quest to bring reproductive freedom to women, Sanger, Pincus and Rock appear to have ignored the implications of shutting down a woman's natural cycle, Kissling explains. In other words, scientists figured out how to supplant periods long before they began trying to understand why they work the way they do.

It was not until the late 1980s that scientists really began to grapple with the larger question of why menstruation happens at all. As an undergraduate, evolutionary biologist Beverly I. Strassmann wrote a paper on how concealing ovulation could entice more paternal partners. (Because a woman's fertile window is more or less invisible, it encourages what researchers call pair-bonding: human males invest in fewer sexual relationships and protect and care for the resulting offspring as a way to ensure their paternity.) Strassmann, now a professor of anthropology at the University of Michigan, wanted to explore human attitudes toward menstruation by collecting data in a community where women spend five nights of their period sleeping in huts that are separate from the rest of the tribe.

In 1986 Strassmann moved to Mali to conduct field research on the Dogon, an ethnic group of millet farmers that hew to their traditions. Dogon people who continue to practice their indigenous religion believe that a menstruating woman's pres-

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ence would desecrate the religious objects in the family compounds. Researchers had not previously considered that these religious beliefs were rooted in any kind of reproductive agenda. But, as Strassmann explains, she hypothesized that this was "a cultural pattern embedded in religion that did directly serve reproduction." Although research on modern indigenous communities can offer only clues about how humans lived thousands of years ago, Strassmann hoped to show that long-standing cultural taboos around menstruation had developed to support our larger evolutionary goals.

During her initial fieldwork, Strassmann studied the community's use of menstrual huts for almost three years, collecting urine samples from 93 women to test hormone levels and prove that their use of the huts correlated with actual menstruation patterns. She also observed how quickly most of the women got pregnant again after their visits to the huts. Although the practice was ostensibly about keeping menstruation sequestered, the huts themselves were located in full view of a shade shelter used by men in the community. So the huts made a woman's fertility status clear to her husband and his family whether she liked it or not. (As noted earlier, women enter their "fertile window" after their period.)

Other religious practices around menstruation, such as the Orthodox Jewish purification ritual of sending menstruating women to mikvah baths, can also be traced to men's need to track female fertility and schedule sexual activity accordingly. And although the advent of the pill means that many women can now control their reproductive life in ways that render the purpose of such practices moot, the taboos still persist, Roberts says. "We still think of menstruation as something that women have to keep hidden and separate."

PERIOD EVOLUTION

ALTHOUGH STRASSMANN'S WORK was primarily about understanding the biological underpinnings of menstrual taboos, her data also revealed important characteristics about the process of menstruation itself. Perhaps her most oft-cited finding was published in 1997 in *Current Anthropology:* across human history, menstruation has been a rather infrequent event. That is because women tend to get pregnant earlier, have more babies and spend more time breastfeeding in communities where birth control is unavailable or difficult to access than they do in communities with high rates of birth-control usage. "We think of periods as happening 12 times a year, but if you're pregnant and then nursing for extended time frames, that's a stretch of two or three years for each child when you're not menstruating," Strassmann explains. Her data showed that in the 1980s the average Dogon woman menstruated only around 100 times in her life, compared with the average American woman's experience of as many as 400 periods in her lifetime. And Dogon women's experience is closer to what all women would have experienced throughout history before the development of the pill.

This historical infrequency of menstruation helps to explain why humans evolved to do something as potentially disadvantageous as releasing blood—losing iron, protein and other nutrients and probably attracting predators in the process. It could also help explain why periods and the week before their onset can be so unpleasant for many women. Michael Gillings, a professor of molecular evolution at Macquarie University in Australia, became interested in women's experiences of premenstrual symptoms (PMS) when premenstrual dysphoric disorder (PMDD) was added to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* in 2013.

PMDD is defined as severe irritability, depression or anxiety in the week or two prior to menstruation, with symptoms easing two or three days after menstruation begins. But Gillings, along with many feminist scholars, balked at the characterization of mood swings as disordered. "Up to 80 percent of women report these symptoms; that makes PMS normal, not a psychological disorder," he says. "So we have to ask, Was there, at some point in history, an advantage to having these symptoms?" In 2014 he published a paper in the journal *Evolutionary Applications* arguing that PMS offered a selective advantage because it caused tension between pair-bonds and therefore might help women dissolve relationships with infertile men. "It is difficult to prove a hypothesis like this," he acknowledges. And the media response characterized him as insensitive to the suffering of women. "I was burned in effigy on five continents," he says. Some researchers counter Gillings's claim that PMS is a product of evolution and contend that its roots are more cultural than biological because it manifests differently around the world. Roberts sees the concept mostly as one influenced by the menstrual taboo and a way to dismiss women's emotions.

Scientists are also divided over whether the act of bleeding itself serves an evolutionary purpose. "It's never made sense to me that we have this free-flowing blood, while other animals reabsorb it," Brown argues. Many evolutionary biologists now think that the essential feature of women's cycles is not the bleeding but rather the ability of the uterus to thicken its lining in preparation for implantation and then dispose of the endometrium when it is not needed. "A healthy endometrium requires constant metabolic support, so it is less energy-intensive for the female body to tear down and rebuild it each cycle than it is to maintain it in a constant state of readiness for embryo implantation," Strassmann explains. Human circulation happens to result in a particularly bloody endometrium. "Our physiology does not permit reabsorption, so much of the blood gets discharged as menstruation," she says. Bleeding may therefore be an insignificant by-product of evolution rather than an advantage.

A WORLD WITHOUT PERIODS?

IF THE ACT OF SHEDDING menstrual blood poses no clear health benefit or evolutionary advantage and if, historically, women have not even done it all that often, then why, in this postpill era, do women continue to do it all? The answer: some do not. In early 2019 the Royal College of Obstetricians and Gynecologists in London released new guidelines that approved skipping the placebo pills in birth control to reduce the frequency of periods or avoid them altogether.

Although this formal acknowledgment is new, the practice is not. Medical menstrual suppression has long been embraced by clinicians, the media and women frustrated by the pain, mood swings or inconvenience of their menstrual cycle. The pharmaceutical industry also took notice: as the researcher who first measured and quantified the frequency of human menstruation, Strassmann has been asked to present her data to drug manufacturers, who have offered several versions of the pill and other

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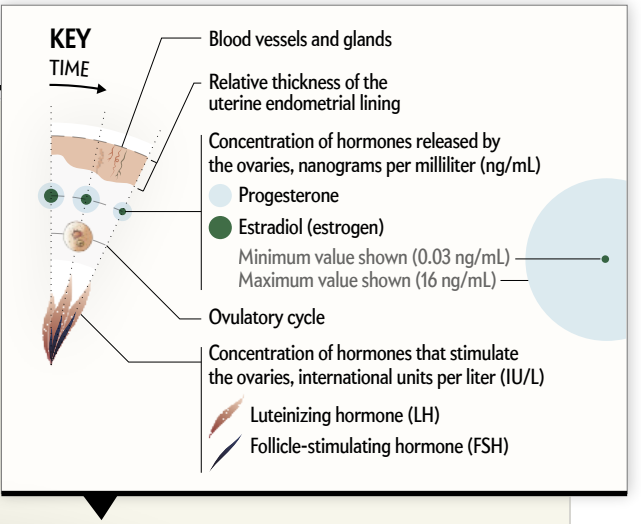
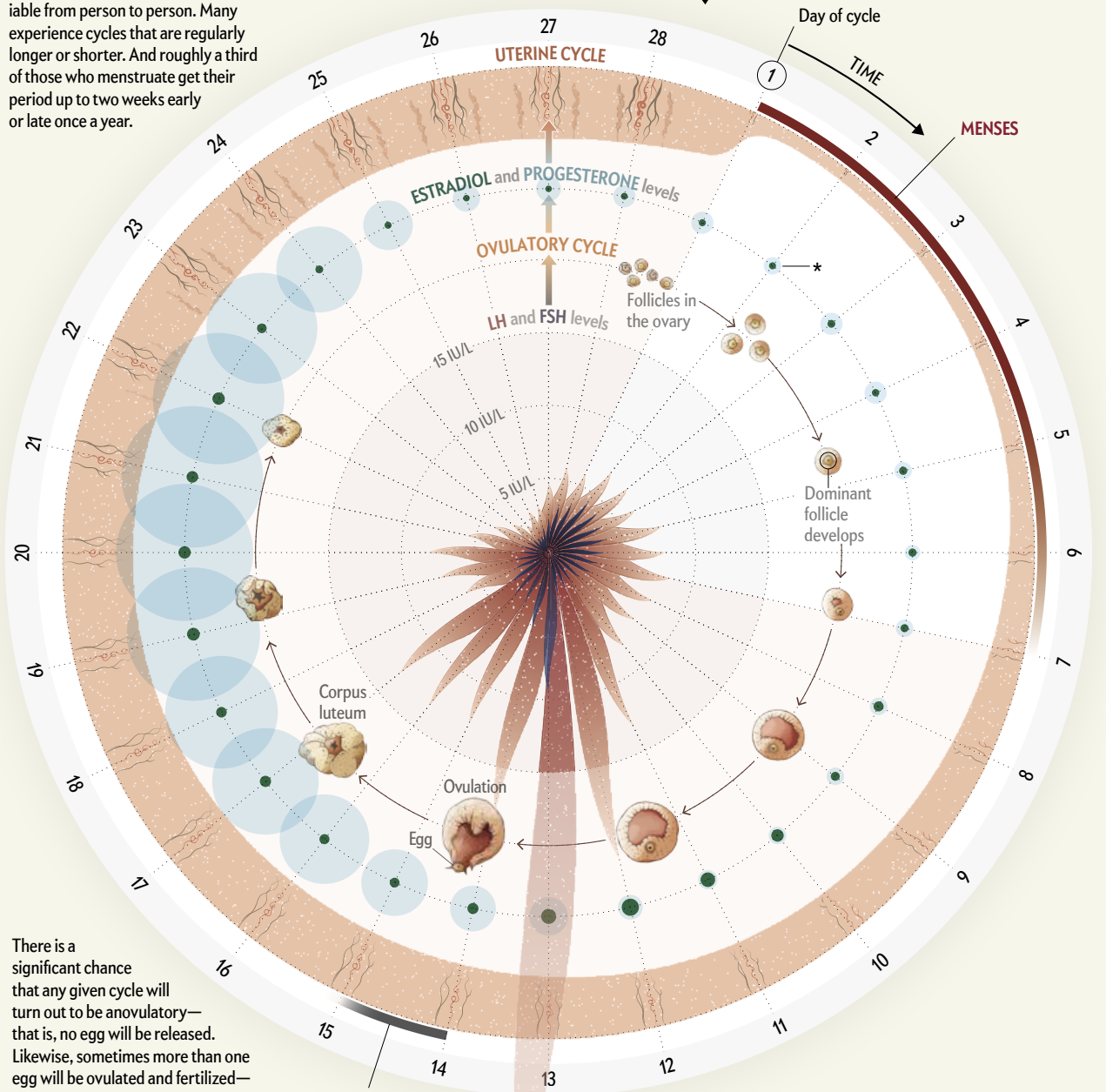
The Menstrual Cycle

Humans are among the very few species to experience a period. The menstrual cycle starts in the brain, which sends signals to the pituitary gland (*not shown*) to produce hormones that stimulate the ovaries. The ovaries house egg-containing follicles that release an egg during ovulation. The ovaries also secrete hormones to help prepare the uterus to host an embryo, which results if the egg is fertilized by a sperm. If no embryo implants, the uterus disposes of its lining, and the cycle begins again.

The average menstrual cycle is 28 days long, but the length is surprisingly variable from person to person. Many experience cycles that are regularly longer or shorter. And roughly a third of those who menstruate get their period up to two weeks early or late once a year.


KEY
TIME
Blood vessels and glands
Relative thickness of the uterine endometrial lining
Concentration of hormones released by the ovaries, nanograms per milliliter (ng/mL)
Progesterone
Estradiol (estrogen)
Minimum value shown (0.03 ng/mL)
Maximum value shown (16 ng/mL)
Ovulatory cycle
Concentration of hormones that stimulate the ovaries, international units per liter (IU/L)
Luteinizing hormone (LH)
Follicle-stimulating hormone (FSH)



There is a significant chance that any given cycle will turn out to be anovulatory—that is, no egg will be released. Likewise, sometimes more than one egg will be ovulated and fertilized—an outcome that can lead to fraternal twins or higher-order multiples.

SOURCE: "CIRCULATING IMMUNOREACTIVE INHIBIN LEVELS DURING THE NORMAL HUMAN MENSTRUAL CYCLE" BY R. I. McLACHLAN ET AL., IN *JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM*, VOL 65, NO. 5; NOVEMBER 1987 (*hormone level data*); JERILYNN C. PRIOR *University of British Columbia, Center for Menstrual Cycle and Ovulation Research (consultant)*

Graphic by Federica Fragapane

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Why Are Girls Getting Their Periods So Young?

Female puberty is starting earlier and earlier, with worrying consequences for women's health

Three weeks before her eighth birthday, Josie got her period at school. Magen, her mother, stopped at a drugstore for supplies before picking up her daughter. In the tampon aisle, she found a shelf of "tween" menstrual pads promising to "fit smaller bodies." She remembers thinking, "How does this even exist as a product?"

Magen was heartbroken that her seven-year-old was menstruating but not completely surprised. She had begun to notice her daughter's body odor when Josie was six. By the time Josie turned seven, she was getting blackheads on her nose, slamming doors and sleeping late. She developed breast buds the summer before second grade. "That was traumatizing for both of us," Magen says.

Magen showed Josie how to put a pad in her underwear and then called the pediatrician, expecting to be referred for some kind of hormonal testing. Instead, Magen recalls, "he said, 'Yes, this happens. She likely won't be regular for a while, but she's very clearly in puberty at eight years old.'"

The average age of menarche, or a girl's first period, in the U.S. is now 12, according to the most recent data from the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey, down from 14 a century ago and as much as six months earlier than 20 or 30 years ago. But puberty does not start with menstruation. The onset of breast development, or thelarche, tends to come first, just as Josie experienced. "We're now seeing thelarche occur 18 months to two years earlier than we did a few decades ago," says Frank Biro, who studies problems related to pubertal maturation at Cincinnati Children's Hospital Medical Center. His research, published in 2013 in the journal *Pediatrics,* put the average age of breast development at 8.8 years old for African-American girls, 9.3 for Hispanic girls, 9.7 for Caucasians and 9.7 for Asian-Americans. "The age of breast development has clearly dropped, while the age of menarche has drifted down. They are both concerning," he says.

One popular misconception about menarche is that it represents the onset of ovulation; in fact, most girls do not begin ovulating regularly for up to two years after their first period, which is why early ones can be light and irregular. Menarche is instead triggered by changes in a girl's estrogen levels. The most probable explanation for why periods and breast development might be happening younger is that girls tend to weigh more today than they did a generation ago—and this higher body fat percentage is leading to earlier activation of the pituitary gland, which produces the hormones responsible for puberty.

In Biro's study, a higher body mass index (BMI) was the strongest predictor of early breast development across all racial groups, although the relation was correlative, not causal. "What we need to ask is, Why has BMI gone up?" he says. "Decreased physical activity and a more calorically dense diet are probably part of the puzzle. But I think another critical piece is our ubiquitous environmental exposure to endocrine-disrupting chemicals," or EDCs. This class of chemicals (including phthalates, bisphenol A and others) is used in many consumer products (shower curtains, plastic bottles, couch cushions) and has been shown to mimic estrogen and other naturally occurring hormones in the human body. Biro theorizes that some of these chemicals may promote weight gain or contribute to early puberty by influencing how cells and the body regulate metabolism, which then affects estrogen production. He is currently leading a study tracking the growth and development of 379 girls from age six onward that has been examining relations between their pubertal development and environmental exposures. Trauma could be another explanation: "Stress can also change your estrogen levels," Biro says.

Josie's mom found a shelf of "tween" menstrual pads promising to "fit smaller bodies." She remembers thinking, "How does this even exist as a product?"

To Magen, the more pressing question is not why Josie started puberty so early but rather what this means for her daughter's immediate and long-term health. The data Biro is collecting now show that girls who start puberty early tend to stay in the stage longer, meaning they spend more time in a "window of susceptibility"—a time when the human body is in a particularly critical stage of development, such that environmental exposures and other experiences are more likely to have an impact on their later health. When it comes to future risk of breast cancer, for example, fetal development and infancy are one window, and puberty is the other. "We know that for every year you delay menarche, you decrease the risk of premenopausal and postmenopausal breast cancer by 4 to 8 percent," Biro says. "On a population basis, that's really important."

Other researchers are looking at how early puberty affects girls socially and emotionally. "We know that early reproductive development is not matched by early cognitive development," says Marcia Herman-Giddens, an adjunct professor of maternal and child health at the University of North Carolina's Gillings School of Global Public Health. "So how do we teach children to manage sexual urges and other realities of puberty? And of course, these girls have to deal with sexual advances from older boys and even men long before they are ready to navigate that."

Magen is trying to figure out how to introduce these issues to Josie in an age-appropriate way without overburdening her already anxious daughter. "I've had to tell her, 'At some point, you're going to feel interested in relationships and sex, and when you are, you need to tell me right away,'" she says. "But am I really going to have to put a 12-year-old on birth control to make sure she's safe?" —*V.S.-S.*

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Continued from page 30

forms of contraception that are formulated to let women skip their periods more often, if not avoid them altogether.

Skipping that monthly ordeal can mean avoiding debilitating pain, prolonged heavy bleeding, migraines and other symptoms that can dramatically impair a woman's quality of life. The approximately 25 percent of reproductive-age women and girls who struggle with additional kinds of severe menstrual pain may be at increased risk for developing other chronic pain conditions. "We suspect the cyclical experience of monthly menstrual pain somehow alters how some women process all kinds of pain," explains Laura Payne, who directs pain research at McLean Hospital and Harvard Medical School.

To many doctors faced with patients whose periods cause problems, "the pill is the closest thing we have to a panacea in women's health," says Jonathan Schaffir, a director at the Ohio State University Wexner Medical Center. But is it? "The pill isn't a treatment for these conditions," Kissling says. "It's a way of refusing to treat them." It can take up to a decade or longer from disease onset for a woman to be diagnosed with endometriosis, for example, in part because doctors are so quick to prescribe the drug to teenagers reporting bad cramps without investigating to see if there is an underlying cause, says endocrinologist Jerilynn C. Prior of the University of British Columbia. And where one version of the pill may succeed in masking a woman's symptoms, another may exacerbate them. "You can spend years jumping from one pill to another, not finding relief," notes Kissling, who published a paper on how women end up "treating each other," for better or worse, in online forums, where they share alternative medicine remedies and other tips out of frustration with their doctors' limited repertoire.

PHONE APPS, such as Clue (*shown*), help women to keep track of their monthly cycles.

Strassmann and many others are skeptical about the health effects of medically induced menstrual suppression, which may expose women to hormone levels higher than what they would have experienced in the evolutionary past or even now, when regularly cycling on the pill. "It's true a monthly menstrual period is not necessary," she says. "But taking more progestin to skip your period is not living like our ancestors did 500 or 1,000 years ago." Research shows taking the pill reduces the risk for endometrial and ovarian cancers but slightly raises the risk for breast cancer, stroke and blood clots.

In 2017 Strassmann and her colleagues published a paper in *Evolution, Medicine, and Public Health* tracking how exposure to synthetic hormones varied depending on the type of birth-control pills used. "We know that American women experience more periods than the Dogon because they start menstruating earlier and have fewer children, and we know that having more periods is associated with a higher breast cancer risk," she explains, noting that the relation is likely because of the additional hormone exposures accrued from those extra periods. "But we don't really know how that risk squares with the hormone exposure women are also getting from long-term use of birth-control pills." After analyzing data from 12 studies, as well as the information on birth-control package inserts, Strassmann's team concluded that some types of the pill exposed women to a quadruple dose of progestin (a synthetic form of progesterone contained in the pill), relative to the progesterone their naturally cycling body would produce.

Nobody knows for sure what that exposure to synthetic hormones will mean long term for women using the pill to suppress their cycles indefinitely. This knowledge gap speaks to broader concerns about our ignorance around menstruation. If Rock and Pincus had begun their work with a deeper understanding of menstruation's evolution and purpose, how might that have affected the pill's development? Would women today have more—and more targeted—options to manage their menstrual pain and associated disorders?

In this latest iteration of our menstrual taboo, dispatching with the period instead of researching its complexity might have unforeseen health consequences, Prior says. "Our data on the pill come from generations of women who followed the schedule for 28-day cycles and didn't stay on it for nearly as long as women do today," Kissling says. "What we have now" with women using birth control for long-term suppression "is the largest uncontrolled medical experiment on women in history." SA

Virginia Sole-Smith is a journalist who writes about feminism, body image and health for the *New York Times Magazine, Harper's Magazine, Elle* and many other publications. She is author of *The Eating Instinct: Food Culture, Body Image, and Guilt in America* (Henry Holt, 2018).

MORE TO EXPLORE

The Biology of Menstruation in *Homo sapiens*: Total Lifetime Menses, Fecundity, and Nonsynchrony in a Natural-Fertility Population. Beverly I. Strassmann in *Current Anthropology*, Vol. 38, No. 1, pages 123–129; February 1997.

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SET IT AND FORGET IT?

The IUD is held up as the gold standard of birth control. That says a lot about the slothful pace of innovation

By Maya Dusenbery

EVEN BEFORE THE RESULTS OF THE 2016 PRESIDENTIAL election were official, women on social media began offering a tip for surviving the next four years: get an IUD tomorrow.

Small, plastic T-shaped devices loaded with synthetic hormones or wrapped with copper coil, IUDs—or intrauterine devices—are inserted into the uterus to offer pregnancy prevention for years. Along with less frequently used hormonal implants that go in the arm, they are known in the reproductive health field as long-acting reversible contraception, or LARC. And with a new leader who pledged to repeal the Affordable Care Act, along with its mandate to cover contraception with no co-pays, many women figured they should seize the chance to secure long-lasting birth control while they still could.

Plenty heeded this advice. Shortly after the election, the president of Planned Parenthood said the organization had seen a "900 percent increase" in IUD-insertion appointments at its clinics nationwide. In March 2019 a study published in *JAMA Internal Medicine* confirmed that the number of women receiving LARC rose by 21.6 percent in the month after Donald Trump won the presidency.

Photographs by Jamie Chung

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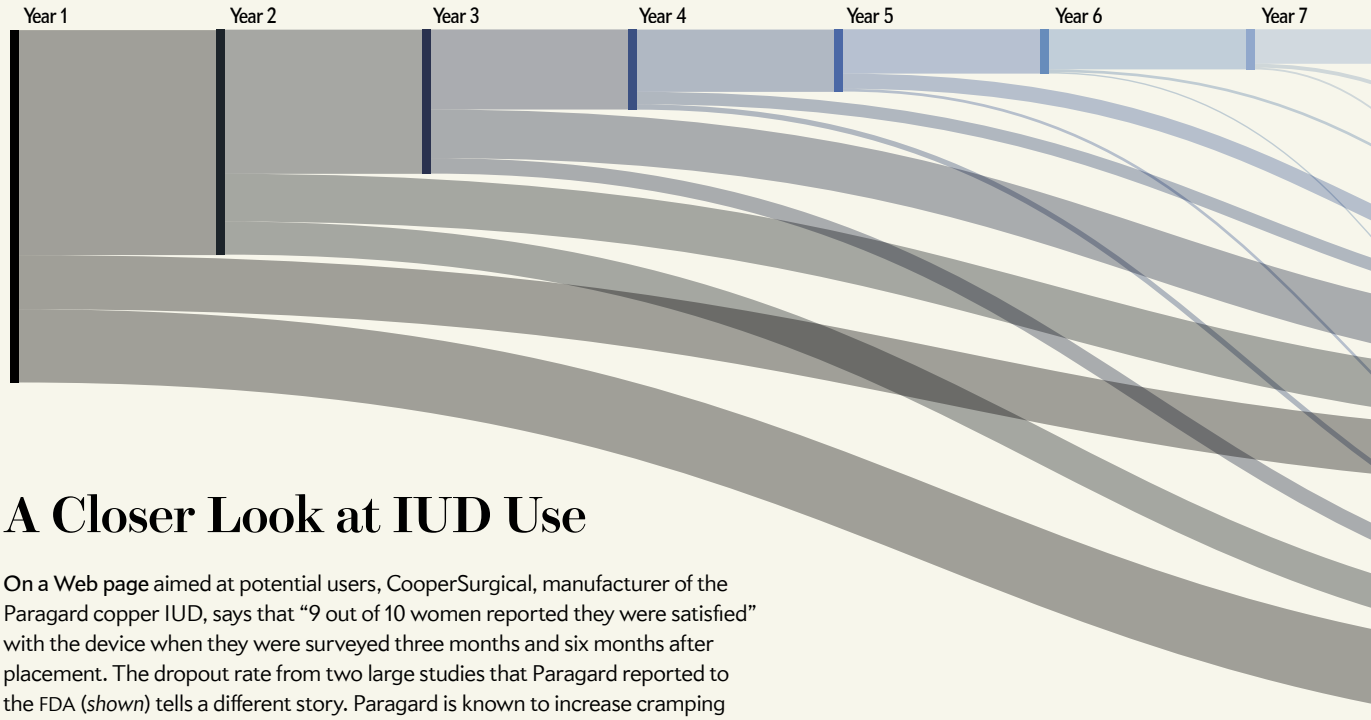

A Closer Look at IUD Use

On a Web page aimed at potential users, CooperSurgical, manufacturer of the Paragard copper IUD, says that "9 out of 10 women reported they were satisfied" with the device when they were surveyed three months and six months after placement. The dropout rate from two large studies that Paragard reported to the FDA (*shown*) tells a different story. Paragard is known to increase cramping and bleeding in many users; a few months may be too short to judge the effects of a device that women live with for years. A 2017 retrospective study of "real-world" IUD discontinuation rates found the number to be even higher.

IN BRIEF

The use of IUDs is at an all-time high and represents a major shift in contraceptive trends.

Although they have very high efficacy rates, many women experience intolerable side effects.

Despite their popularity, IUDs may be the least of multiple evils, highlighting the dearth of birth-control options available to women.

While this so-called Trump bump was significant, the comeback of IUDs began several years earlier. In 2002 just 2 percent of U.S. women using contraception chose them. In 2014 that number rose to 11.8 percent, an all-time high that matches the average prevalence among other developed nations. For decades IUDs had a bad image after the Dalkon Shield, a poorly designed device from the 1970s, caused infections, infertility and even death in tens of thousands of women. Today's models are much safer, and younger women don't have the same negative associations with IUDs as prior generations. Before 2010 the high up-front cost of such a device—up to several hundred dollars—was often a nonstarter. But under the still intact Affordable Care Act, insertion is free with private health insurance.

IUDs have also benefited from a concerted advocacy effort to eliminate barriers to their use. A Colorado outreach initiative to provide low-income women with no-cost IUDs and implants, which was launched in 2009, led to significant declines in the state's teen birth and abortion rates and drew national attention. Since 2014 a nonprofit called Upstream has offered training and technical assistance to health centers to increase same-day access to all forms of birth control, particularly LARC. Upstream currently partners with state governments in Delaware, Massachusetts, Washington State and North Carolina. Under the program, use of IUDs and implants among low-income women in Delaware more than doubled in three years. Forty states have now changed their Medicaid policies to reimburse hospitals for inserting IUDs in the delivery room immediately postpartum.

The rising popularity of the IUD represents the largest shift in American contraceptive trends in recent decades. Researchers at the Guttmacher Institute say it has contributed to an 18 percent decrease in the unintended pregnancy rate between 2008 and 2011: a "historic" low after a long period of stagnation. Both the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics now recommend IUDs as a top birth-control option for all women, including adolescents.

It's easy to see why IUDs are so appealing: less than 1 percent of users will get pregnant in a year, making the devices just as effective as sterilization, and they last between three and 12 years. What gives IUDs the most compelling edge over other methods is that they are practically immune to human error. Once inserted, you don't have to do anything else—interrupt sex to put on a condom or remember to take a pill at the same time every day—to get reliable pregnancy prevention. It is this feature in particular that has led to a common refrain in the reproductive

SOURCE: PARAGARD® T380A INTRAUTERINE COPPER CONTRACEPTIVE. PRESCRIBING INFORMATION. TEVA WOMEN'S HEALTH. SUBMITTED TO FOOD AND DRUG ADMINISTRATION ON JUNE 11, 2013

Graphic by Amanda Montañez

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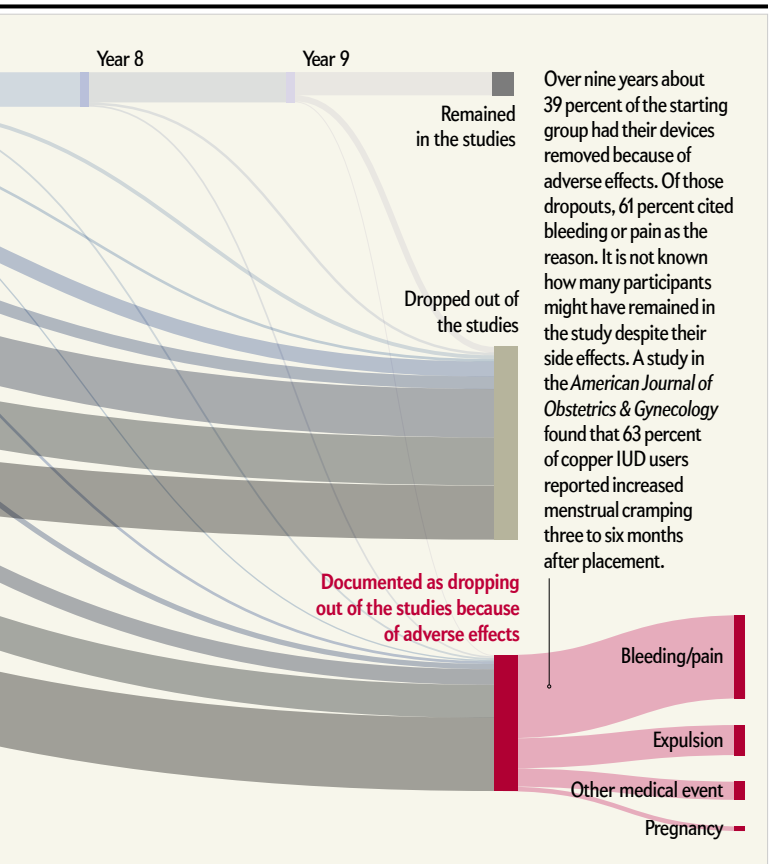
Year 8
Year 9
Remained in the studies
Dropped out of the studies
Documented as dropping out of the studies because of adverse effects
Bleeding/pain
Expulsion
Other medical event
Pregnancy
Over nine years about 39 percent of the starting group had their devices removed because of adverse effects. Of those dropouts, 61 percent cited bleeding or pain as the reason. It is not known how many participants might have remained in the study despite their side effects. A study in the American Journal of Obstetrics & Gynecology found that 63 percent of copper IUD users reported increased menstrual cramping three to six months after placement.

health field: "Set it and forget it," an Upstream trainer recently told the *New York Times,* borrowing the advertising tagline of a rotisserie chicken oven to describe the IUD.

On the surface, this highly effective, long-acting, difficult-to-mess-up form of birth control seems to be well liked. ACOG's guidelines point out that IUDs have the highest continuation rates and user satisfaction of all reversible birth-control methods. Diana Blithe, program director for contraception development at the National Institutes of Health's National Institute of Child Health and Human Development (NICHD), says the introduction of the first hormonal IUD in 2000, in particular, "has been a bit of a game changer in that women like it." Three fourths of IUD users in the U.S. choose a hormonal IUD (as opposed to the nonhormonal copper IUD), which tends to make menstrual periods lighter or disappear altogether. "It's really effective and popular—it's all good," Blithe says.

There are plenty of self-described IUD evangelists. But that's not the whole picture. Although IUDs do work well for many women, a significant number experience side effects and sometimes debilitating ones. As medical devices, IUDs have drawbacks that other contraceptive methods do not. Without easy access to a health care provider—and one who takes a patient's symptoms seriously—"set it and forget it" can start to sound less like convenience and more like coercion.

The IUD cheerleading obscures a broader illusion of choice. Nearly 60 years after the first oral contraceptive pill was sold, most prescription birth-control methods are variations on the same synthetic hormones that have always been used. The first IUDs date back even further, to a time when inert devices made of silkworm gut or metal stopped pregnancy by creating sustained inflammation. At a time when lawmakers are constantly threatening to roll back access to all aspects of reproductive health care, it can feel risky to criticize birth-control methods. After all, ultraconservative foes of birth control tend to manipulate concerns about side effects and risks into a reason women should forgo contraception entirely. But in 2020 it is worth asking: Why don't we have more innovative birth-control options? When it comes to preventing pregnancy, is a device that works in part by irritating the uterus really the best science can provide?

MEASURING DISSATISFACTION

MUCH OF THE RECENT ENTHUSIASM over IUDs can be traced back to a single study called the Contraceptive CHOICE research project. Funded in part by a then anonymous donor now known to be the Susan Thompson Buffett Foundation and facilitated by Washington University in St. Louis, the project had the explicit goal of increasing the use of LARC among women at high risk of unintended pregnancy.

Between 2007 and 2011 a cohort of 9,256 women and adolescent girls were offered their choice of a contraceptive method free of charge. Participants received "tiered contraceptive counseling," in which they were presented with the risks and benefits of each method in order of most effective to least effective, meaning that they heard about IUDs and implants first. Three quarters of the participants chose to use those LARC methods, and those who did were 20 times less likely to have an unintended pregnancy than those who chose other prescription methods such as the pill.

In addition to this dramatic effect on unintended pregnancy rates, the reproductive health field was excited by the discontinuation rates found in the CHOICE study. The number of women who had their IUD or implant removed early was much lower, relative to the study participants who had abandoned their non-LARC methods. Remarkably, 69 percent of the women who had chosen oral contraceptives, injection, the vaginal ring or the skin patch had given up on them after three years—more than twice the dropout rate of the IUD users. As such, the IUD was held up as the form of birth control that users liked the most.

But what is often underdiscussed are the IUD discontinuation rates themselves. After one year nearly 20 percent of copper IUD users and about 14 percent of hormonal IUD users reported they were "not satisfied" with the device; 12.5 and 16 percent, respectively, had had it removed. Around the five-year mark, 44.1 percent of copper IUD—and 48.3 percent of hormonal

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IUD—users had discontinued the device. About two thirds of those who had done so by the end reported that the reason was because of pain, bleeding changes or other side effects or because the foreign object had been expelled from their body. In other words, the IUD dropout rate linked to side effects looks low largely in the context of other methods.

The CHOICE findings, which have been reported in nearly 70 published papers and more than 500 media outlets, helped to spur a shift in the field from "options-based" contraceptive counseling, in which a range of methods are presented, to the "LARC-first" counseling used in the CHOICE study. Even the ACOG guidelines cite the CHOICE study as evidence of the "superiority of LARC methods over short-acting methods." Manufacturer brochures for IUDs, such as from CooperSurgical, manufacturer of Paragard, also use CHOICE data to promote their devices to women.

Other studies have reported markedly higher discontinuation rates. In the original Food and Drug Administration clinical trials, the five-year rates for the copper Paragard and hormonal Mirena were 60 and 55 percent, respectively. Then, in 2017, a retrospective study at Harvard Medical School of more than 1,000 American women found that at five years, 71.9 and 76.2 percent, respectively, had removed their device. The researchers suggested that these results might better reflect "real-world" rates in the clinical setting, "outside of the structured setting of a randomized controlled trial," or the CHOICE study, which was trying to increase uptake of LARC and offered subjects "extensive counseling."

That IUDs are comparatively well liked might say less about how popular they are and more about how dissatisfied women are with birth control in general. Perhaps the IUD is just the least onerous option out of an unimpressive field. According to an analysis of data from the 2006–2010 National Survey of Family Growth, women in the U.S. have tried a median of three contraceptive methods. Whereas many women eventually find one that works well for them—often after years of trial and error—some simply settle on one out of sheer frustration: nearly two fifths of women surveyed in 2004 by the Guttmacher Institute said they chose their current method mostly because they didn't like any other available options.

It is hard to know what self-reported "satisfaction" is even measuring when it comes to contraception. "Many women tolerate negative side effects because their sense of the risk of pregnancy is higher or their anticipation of the consequence of a pregnancy is worse," says Diana Greene Foster, director of research at Advancing New Standards in Reproductive Health (ANSIRH) at the University of California, San Francisco. Nearly 40 percent of women in the Guttmacher survey said they were not satisfied with the method they were currently using. And that makes them less likely to use it consistently. For example, 48 percent of dissatisfied oral contraceptive users skipped at least one pill in the past three months as compared with 35 percent of satisfied users.

Just how far we are from having a variety of options that truly meet women's needs becomes clear when you ask them what they actually *want* in a contraception method, which Foster and her colleagues did in a 2012 study. The three features deemed "extremely important" by the largest proportions of women were effectiveness (84 percent), lack of side effects (78 percent) and affordability (76 percent). Then they determined how many of the currently available methods met the women's criteria and found that "for 91 percent of women, no contraceptive method has all the features they think are extremely important." Perhaps unsurprisingly, what women really want is a highly effective method with few or no side effects. And as the researchers explain in the study, "that combination does not exist."

The IUD discontinuation rates seem more notable after considering how much harder it is to stop using a device that is lodged in your uterus than it is to stop taking a pill. The process of removing an IUD is often no more complicated than pulling on the exposed strings, and some researchers have begun to explore how to make self-removal more feasible. But for now IUD extraction requires an appointment with a health care provider—an appointment that some women struggle to access or afford. Even then, several qualitative studies have found that many women who want to stop using their IUD because of side effects face resistance from their doctor.

In a pair of recent studies, Jennifer R. Amico, an assistant professor at Rutgers Robert Wood Johnson Medical School, and her colleagues interviewed providers and women seeking "early" IUD removal—within nine months of insertion—at two clinics in New York City. Many of the women said their providers minimized their side effects and were reluctant to grant their request for removal. The providers, many of whom admitted they had negative feelings about early removals, said they usually encouraged patients to stick with the device for at least three to six months.

The belief that side effects will improve for most IUD users after an "adjustment period" is widely held by providers. But most studies claiming to show such a decline in side effects over time have not accounted for the dropping out of dissatisfied users. In other words, it could be an illusion produced by the fact that those who do continue to have side effects eventually remove the device, leaving only satisfied users at the end. In a 2009 prospective analysis of copper IUD users that sought to correct this bias in prior studies, researchers found that while some problems improved, others did not; women reported that the number of days they experienced spotting and pain between periods actually became *more* frequent over time.

"There is a long, terrible history of discounting what women report as contraceptive side effects," Foster says. In the 1950s, when the first large human trials of the original birth-control pill—which contained

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astronomical levels of hormones by today's standards—were conducted on Puerto Rican women, their complaints of severe side effects were brushed off as hypochondria. Today, Foster says, "there is a belief that if a clinician tells a woman about side effects, that she is more likely to experience them." Indeed, a number of published articles in recent years claim that "nonspecific" side effects to oral contraceptives are the result of the "nocebo" effect—a negative placebo effect—and so providers should offer "optimistic" counseling that downplays their likelihood.

THE ILLUSION OF CHOICE

THE "LARC-FIRST" MOVEMENT is based on the assumption that effectiveness should be the only factor to consider in a contraceptive method. "Folks will often say, 'I wouldn't give you a statin that is 91 percent effective versus one that is 99 percent, so why would I give a contraceptive that has that difference in efficacy?'" says Anu Manchikanti Gomez, director of the University of California, Berkeley's Sexual Health and Reproductive Equity Program. But there are many factors—from side effects to health risks to control over starting and stopping the method—that women weigh when choosing among imperfect options.

Gomez, who co-authored a critique of the LARC zeal in a 2014 article entitled "Women or LARC First?" now says that the reproductive health field has begun to see a "pendulum shift toward a patient-centered approach and recognition that what health care providers and policy makers consider to be the 'best method' is often misaligned with what women want." In 2016 the advocacy groups National Women's Health Network and SisterSong released a statement of principles for IUDs and implants that rejected "efforts to direct women toward any particular method" while supporting greater access to LARC devices. It also emphasized the right of all women to opt against LARC or discontinue using one without judgment from their provider. More than 250 advocates and organizations, including ACOG, have signed on to it.

The reality is that most women who are shopping for birth control likely won't choose these devices anyway. In a 2015 study, Foster and her team surveyed about 100 experts who had published research on LARC and asked them to estimate how many women would use it if all the current barriers were eliminated. The median estimate was 25 percent. "The idea that LARCs are going to solve all our problems is problematic on a lot of fronts," Foster says. "It's also just not realistic." The solution to better birth control, she adds, lies in soliciting and respecting women's preferences when it comes to contraception and then using science to develop methods that meet their needs.

That is certainly not the approach we have taken so far. Although investment in research and develop-

BARRIERS don't have side effects, but hormones are more effective. This variety of choice is really a study in trade-offs.

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ment by pharmaceutical companies in the 1990s and 2000s yielded new products, such as the patch, ring and hormonal IUD, it has cooled in the past decade. These days "they think that there are enough products for female contraception," says Régine Sitruk-Ware, a scientist at the Population Council's Center for Biomedical Research.

Anyway, recent contraception advances have largely been tweaks to the formulations or modes of delivery of the same basic synthetic hormones that have always been used. And projects in the pipeline are similarly focused on making existing contraceptives easier or safer. For example, a self-administered injectable, recently approved in other countries, could hit the market in the U.S. A "pericoital" pill, similar to emergency contraception, that needs to be taken only when someone has sex is under development. So is a ring that uses natural estradiol—bioidentical to the estrogen in the human body—instead of a synthetic estrogen, which may be a safer option for women put at an increased risk of blood clots by many existing hormonal contraceptives.

THAT IUDS ARE COMPARATIVELY WELL LIKED MIGHT SAY LESS ABOUT HOW POPULAR THEY ARE AND MORE ABOUT HOW DISSATISFIED WOMEN ARE WITH BIRTH CONTROL IN GENERAL.

Experts say the focus has been on improving existing hormonal methods largely because they are well understood at this point. Efforts to develop brand-new ones will face a long and expensive path to reach the market. But all the scientific progress since the pill was developed could yield much more imaginative strategies.

TOWARD INNOVATIVE BIRTH CONTROL

RECENT ADVANCES in genomics have identified many proteins, enzymes and genes involved in the reproductive process that could be targeted to prevent pregnancy in both women and men—and potentially do so in more precise ways. Sitruk-Ware says her group is exploring a molecule that, by acting on a particular protein, would prevent sperm from maturing, making them unable to fertilize an egg. Another research team has been testing a compound in nonhuman primates that binds to a different protein and turns off sperm's ability to swim. "There may be as many as 1,000 possible targets," Blithe says, including some "very exciting possibilities" when it comes to inhibiting ovulation that are at the basic research stage.

None of these compounds has made it through preclinical toxicology studies to get into a human trial yet. "We are expecting that they would be safer because we are targeting and blocking only one specific protein, and there will be no other action on any other cells in the human body," Sitruk-Ware says. "But it's unknown—any molecule may bring other effects."

Genomic approaches could someday bring a precision medicine approach to prescribing contraception as well. Genetic variations may explain why the side effects of contraceptive methods vary widely among individuals—and genetic testing might help predict which method is best for a particular woman. For example, although such testing is not available in routine practice, doctors already have the ability to test for specific mutations that put women at higher risk of blood clots on estrogen-based contraceptives. And genetic variations may explain why no birth control is 100 percent foolproof. A study published online in March 2019 in *Obstetrics & Gynecology* found that about 5 percent of women possess a genetic mutation that makes them more likely to produce an extra hormone-dismantling enzyme that makes birth control less effective. Previously, women who got pregnant on the pill were blamed for not using it correctly.

Technological advances are also bringing more precision to one of the oldest contraceptive methods: fertility awareness. A couple can fertilize an egg only up to about five days before and two days after ovulation because of the combined viability of sperm and egg in the female body. So the goal of fertility awareness-based methods, or FABMs, is to predict—and then confirm—when ovulation occurs. Many FABMs do so by tracking physical signs of hormonal shifts, including changes in cervical fluid and a spike in basal body temperature. When done right, some are 95 to 99 percent effective.

FABMs are one of the only contraceptive methods besides LARC whose popularity is on the rise. An estimated 3.2 percent of women using contraception use a FABM today, a figure that doubled between 2008 and 2014. The interest is likely being driven in part by the variety of fertility- and period-tracking apps now available. Some just provide a digital platform to chart one's cycle, whereas others utilize predictive algorithms. "There's machine learning going on in the app that helps it adapt to the woman's cycle," explains Victoria Jennings, director of the Institute for Reproductive Health at Georgetown University Medical Center.

Jennings doubts the new algorithm-based apps are *more* effective than old-school FABMs that require a woman to chart her cycle with paper and pencil, but "they're so much easier to use that, in my opinion, people may be more likely to use them correctly." So far few apps have undergone rigorous efficacy testing. She and her colleagues recently completed a first-of-

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its-kind prospective study of one such app called Dot. The results, published online in March 2019 in the *European Journal of Contraception and Reproductive Healthcare,* found a perfect-use failure rate of 1 percent and a typical-use failure rate of 5 percent.

Even with an app, FABMs are as far from "set it and forget it" as you can get. Because a woman's cycle is affected by factors such as stress, lack of sleep and illness, algorithms cannot confidently predict the exact day of ovulation for each cycle based on historical patterns alone. That is where scientific advances could help. Current at-home urine tests can anticipate ovulation by a couple of days at most. But that won't cut it if a couple is trying to avoid pregnancy instead of achieve it. "I would love to see some kind of a hormonal test that could accurately predict ovulation far enough in advance for people to be able to rely on it for pregnancy prevention at a cost that they could afford," Jennings says. That would achieve the same goal as FABMs at a fraction of the effort.

Of course, one way to relieve some of the burden on women to prevent pregnancy is to share it with their male partners. Hormonal birth control for men is much further along in development than nonhormonal approaches for either sex. "We have a lot of small studies that demonstrate it works and in a similar way to female methods," Blithe says. Late in 2018 the second phase of a clinical trial of 420 couples to test the safety and efficacy of a male contraceptive gel, developed by the Population Council and NICHD, got underway. But the oft-repeated joke in the field is that male contraception has been 10 years away for 30 years. "I'm not promising anything in the next five years for men," Blithe says.

Among the barriers to developing a male contraceptive has been that the regulatory pathway is uncertain. When the FDA evaluates the safety of a female contraceptive method, any health risks are compared with the risks the woman could experience from pregnancy to calculate the risk-benefit ratio. But in the case of a male contraceptive, "the FDA is going to have a very high bar, I'm sure, when it comes to getting approval for a drug that will be taken by the person who is not at risk of pregnancy," Blithe says. The pharmaceutical industry has also yet to be convinced there is a big market. A 2005 survey of men in nine countries found that 55 percent would be willing to use a male hormonal contraceptive. (Their current options are only condoms and vasectomy.) More recent market research by the Male Contraceptive Initiative found almost four in 10 men in the U.S. would be interested, but they also reported "little tolerance for side effects," especially depression, reduced libido or acne.

Researchers acknowledge that a male contraceptive may need to meet a higher standard than its female counterparts. To many women, the benefit of pregnancy prevention is great enough that they're willing to put up with nausea, mood swings or heavier periods as the trade-off. "But men? Not necessarily," says Sitruk-Ware, who co-founded the International Consortium of Male Contraception. "If they make this effort of taking the burden of the couple's contraceptive method, they would expect that there are absolutely no side effects."

Female contraceptives should have to clear that high bar, too. Birth control, in general, presents a more complicated risk-benefit analysis than other medications. In exchange for treatment for a life-threatening illness, people may accept considerable side effects and health risks. But "contraceptives are not designed to treat a disease, and the users are typically young and healthy," Sitruk-Ware says. "Zero side effects should be the rule."

This push for contraceptive innovation is not universally evident. Many investors believe that to reduce unintended pregnancies, we simply need to ensure that women have access to existing methods. But dissatisfaction is also a reason people use contraception inconsistently or forgo it entirely. Safeguarding and expanding access, though vital, need not crowd out the pursuit of better birth control—a truly diverse range of options that meet the differing needs of both women and men at various stages in their reproductive lives. "Adolescents may not want the same method as a woman who is spacing her pregnancies or a woman who has completed her family," Sitruk-Ware says. Likewise, whereas many women in a committed relationship may consider a male contraceptive a welcome relief, for others, maintaining control themselves over the use of the method is paramount.

It is hoped that researchers—and funders—will develop targeted ways of preventing pregnancy, along with the ability to more precisely match formulations to individuals' unique physiology. For now a more personalized approach is critical to help women choose among the current lineup of choices, which force too many of us to trade well-being for effectiveness. Finding a contraceptive method that best fits someone's body, way of life and priorities is a complex task—and shouldn't be compared to setting a chicken in an oven and walking away. SA

Maya Dusenbery is a journalist and author of *Doing Harm: The Truth about How Bad Medicine and Lazy Science Leave Women Dismissed, Misdiagnosed, and Sick* (HarperOne, 2018). Previously she worked at the National Institute for Reproductive Health.

MORE TO EXPLORE

Association of Short-Term Bleeding and Cramping Patterns with Long-Acting Reversible Contraceptive Method Satisfaction. Justin T. Diedrich et al. in *American Journal of Obstetrics and Gynecology,* Vol. 212, No. 1, pages 50.e1–50.e8; January 2015.

Preventing Unintended Pregnancy: The Contraceptive CHOICE Project in Review. Natalia E. Birgisson et al. in *Journal of Women's Health,* Vol. 24, No. 5, pages 349–353; May 14, 2015.

FSRH Guideline: Combined Hormonal Contraception. Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynecologists, January 2019 (amended July 2019). www.fsrh.org/standards-and-guidance/documents/combined-hormonal-contraception. www.fsrh

scientificamerican.com/magazine/sa

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How to Reduce Maternal Mortality

To prevent women from dying in childbirth, the first step is to stop blaming them

Text by Monica R. McLemore, Graphics by Valentina D'Efilippo

THE SHAMEFUL SECRET IS OUT: ALTHOUGH THE NUMBER OF WOMEN who die in childbirth globally has fallen in recent decades, the rates in the U.S. have gone up. Since 1987 maternal mortality has doubled in the U.S. Now approximately 800 maternal deaths occur every year. One of the most striking takeaways from examining the data is racial disparity: Black women are three to four times more likely to die from pregnancy-related conditions such as cardiac issues and hemorrhage and to bear the brunt of serious complications as well. That risk is equally shared by all black women regardless of income, education or geographical location. In other words, the factors that typically protect people during pregnancy are not protective for black women.

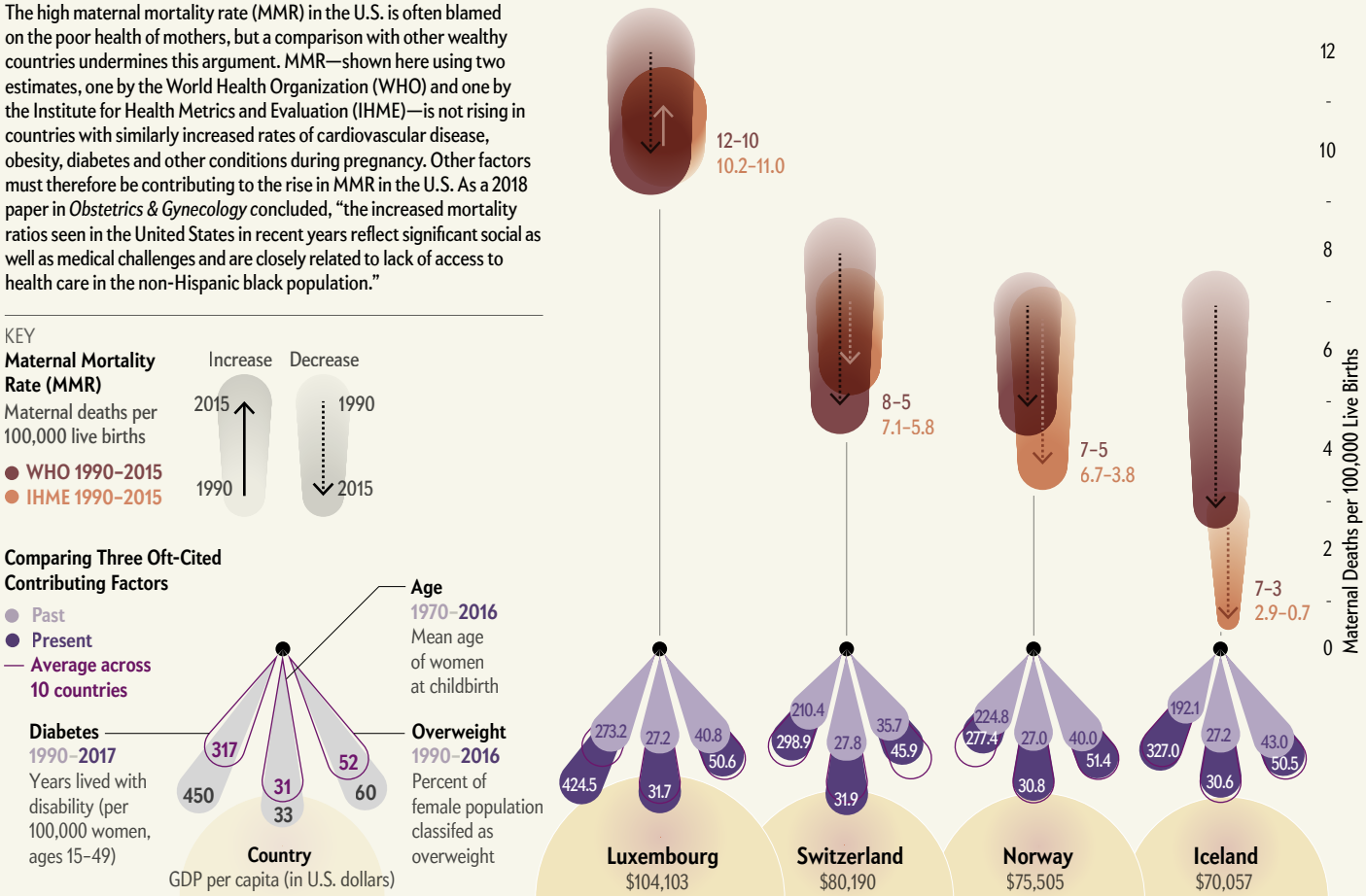
Fortunately, most of these deaths are considered preventable, and therefore, much more can be done to stop them. First, everyone—from doctors to the media to the public—needs to stop blaming women for their own deaths. Instead we should focus on better understanding the underlying contributing factors. These include a lack of data; not educating patients about signs and symptoms—and not believing them when they speak up; errors made by health care providers; and poor communication among different health care teams. Finally, studies have shown that interventions such as wider access to midwifery, group prenatal care, and social and doula support are effective in improving maternal health outcomes.

Progress has been slow and uneven. Deaths from hemorrhage, for example, have been reduced by half in some states because of standardized tool kits for care. And California has led in the pursuit of understanding root causes of maternal mortality. Still, structural racism is proving to be an intractable force. SA

Monica R. McLemore is an assistant professor in the family health care nursing department and a clinician-scientist at Advancing New Standards in Reproductive Health at the University of California, San Francisco. She maintains a clinical practice at Zuckerberg San Francisco General.

The U.S. Is an Outlier

The high maternal mortality rate (MMR) in the U.S. is often blamed on the poor health of mothers, but a comparison with other wealthy countries undermines this argument. MMR—shown here using two estimates, one by the World Health Organization (WHO) and one by the Institute for Health Metrics and Evaluation (IHME)—is not rising in countries with similarly increased rates of cardiovascular disease, obesity, diabetes and other conditions during pregnancy. Other factors must therefore be contributing to the rise in MMR in the U.S. As a 2018 paper in *Obstetrics & Gynecology* concluded, "the increased mortality ratios seen in the United States in recent years reflect significant social as well as medical challenges and are closely related to lack of access to health care in the non-Hispanic black population."



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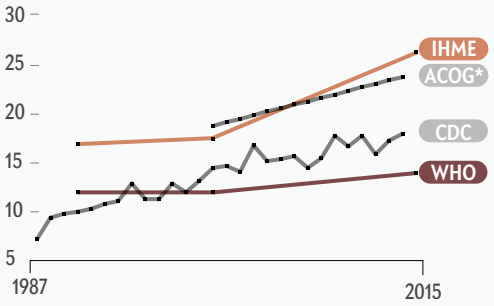
U.S. Maternal Mortality Rate Estimates

According to different organizations



Inconsistent Data Collection across the States

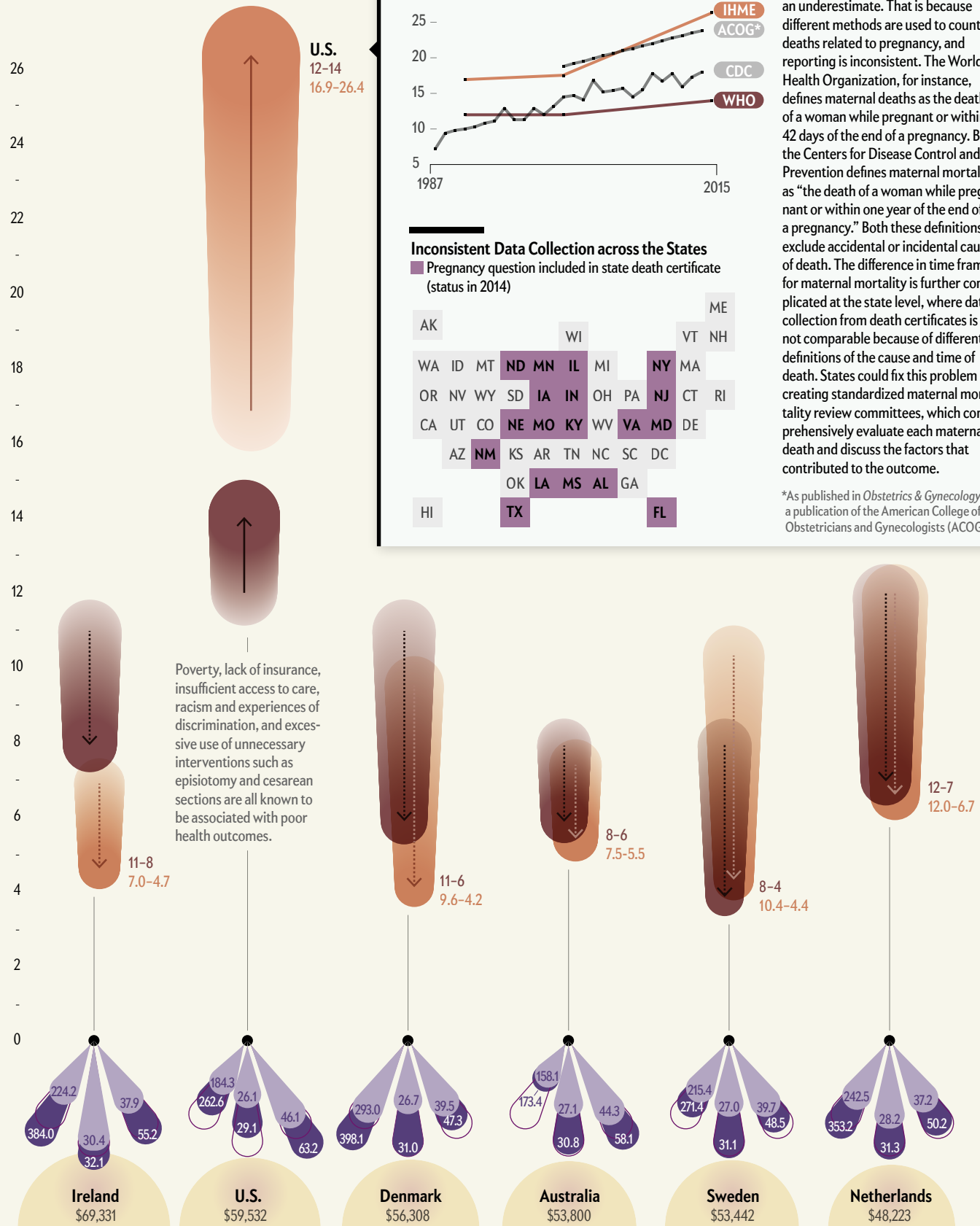
Pregnancy question included in state death certificate (status in 2014)

									ME	
AK					WI				VT	NH
WA	ID	MT	**ND**	**MN**	**IL**	MI		**NY**	MA	
OR	NV	WY	SD	**IA**	**IN**	OH	PA	**NJ**	CT	RI
CA	UT	CO	**NE**	**MO**	**KY**	WV	**VA**	**MD**	DE	
	AZ	**NM**	KS	AR	TN	NC	SC	DC		
			OK	**LA**	**MS**	**AL**	GA			
HI			**TX**					**FL**		

Maternal Mortality Data in the U.S. Are an Unreliable Mess

As bad as the numbers sound, the U.S. MMR is widely considered to be an underestimate. That is because different methods are used to count deaths related to pregnancy, and reporting is inconsistent. The World Health Organization, for instance, defines maternal deaths as the death of a woman while pregnant or within 42 days of the end of a pregnancy. But the Centers for Disease Control and Prevention defines maternal mortality as "the death of a woman while pregnant or within one year of the end of a pregnancy." Both these definitions exclude accidental or incidental causes of death. The difference in time frame for maternal mortality is further complicated at the state level, where data collection from death certificates is not comparable because of different definitions of the cause and time of death. States could fix this problem by creating standardized maternal mortality review committees, which comprehensively evaluate each maternal death and discuss the factors that contributed to the outcome.

*As published in *Obstetrics & Gynecology*, a publication of the American College of Obstetricians and Gynecologists (ACOG).



SOURCES: GLOBAL HEALTH OBSERVATORY DATA REPOSITORY, WORLD HEALTH ORGANIZATION (*WHO MMR data*); MATERNAL MORTALITY 1990–2015 TABLES IN *GLOBAL BURDEN OF DISEASE STUDY 2015*. GLOBAL BURDEN OF DISEASE COLLABORATIVE NETWORK. INSTITUTE FOR HEALTH METRICS AND EVALUATION, 2016 (*IHME MMR data*); IHME (*diabetes*); ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (*age*); WHO (*weight*); WORLD BANK (*GDP*); "RECENT INCREASES IN THE U.S. MATERNAL MORTALITY RATE: DISENTANGLING TRENDS FROM MEASUREMENT ISSUES," BY MARIAN MACDORMAN ET AL., IN *OBSTETRICS & GYNECOLOGY*, VOL. 128, NO. 3; SEPTEMBER 2016 (*ACOG data and map*)

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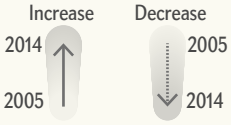
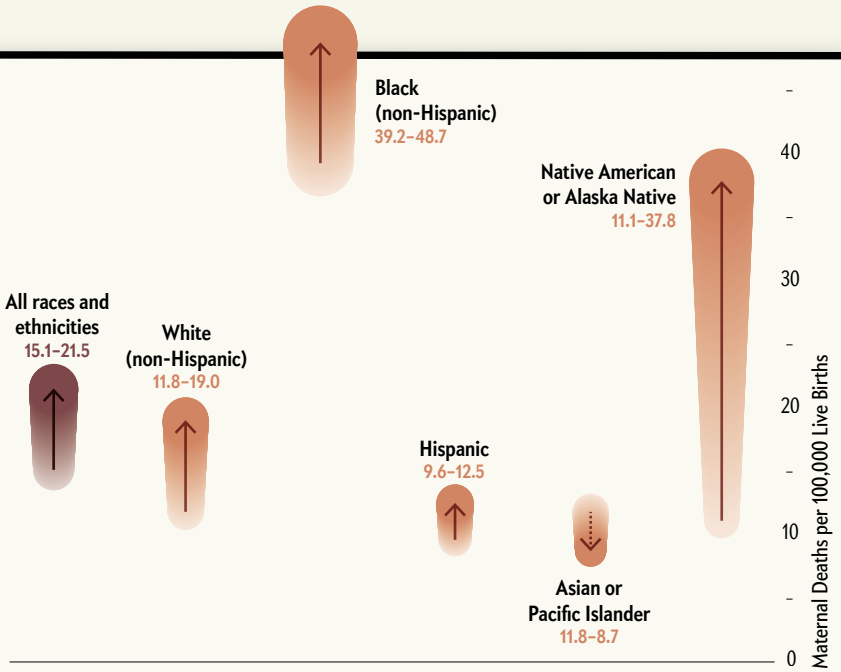
Who Is Dying?

It's common to blame women for their own deaths. Many scientific publications have cited that women are coming to pregnancy older (called advanced maternal age, or geriatric pregnancy), sicker (with hypertension, diabetes or other chronic illnesses) and fatter (that is, suffering from obesity). But even in studies that control for age, chronic disease and obesity, the MMR in the U.S. still far exceeds rates in similarly wealthy nations. In a 2016 report that looked at pregnancy-related death disparities among states, the authors wrote that "excellent care is apparently available but is not reaching all the people."

U.S. Maternal Mortality Rate over Time, by Race and Ethnicity

2005–2014

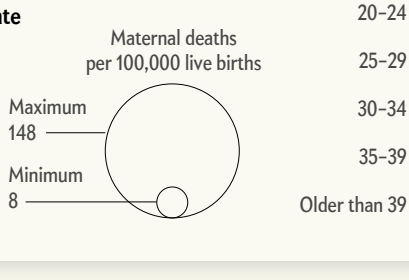


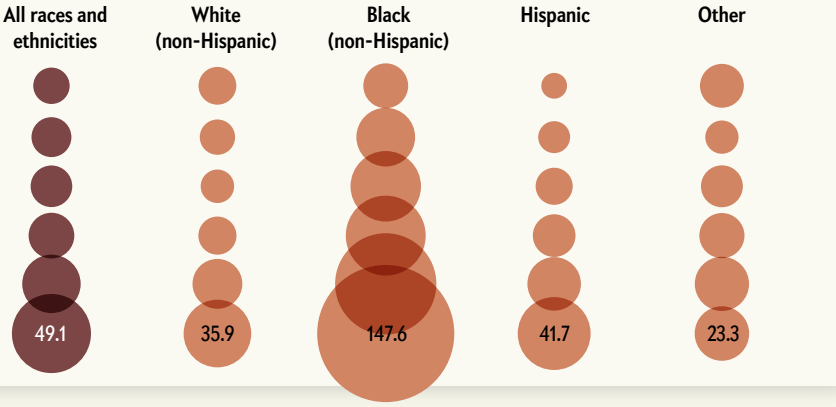


In all racial categories, maternal mortality is worse among older women, but the burden is concentrated among black women, who are more likely to experience structural determinants of health that worsen over time.

U.S. Maternal Mortality Rate across Age Groups

2006–2010



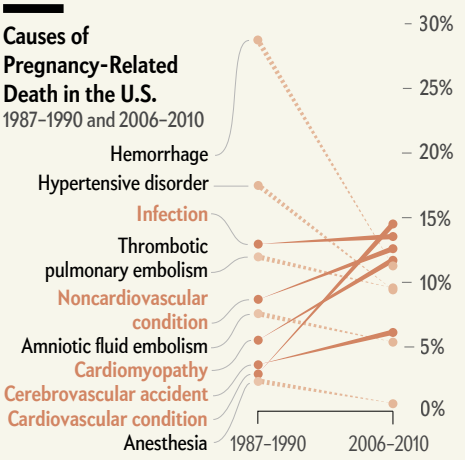


Why Are Mothers Dying—and How Many Causes Are Preventable?

Pregnancy exacerbates existing clinical conditions such as cardiovascular disease (including high blood pressure), enlarged heart and an irregular heartbeat. Black women are more likely to have these conditions before, during and after pregnancy. Chronic, toxic stress—the way that experiences of discrimination are embodied—has been shown to make these conditions worse. But in the U.K., for example, there were only two deaths from preeclampsia and eclampsia over a three-year period, according to a 2018 study, suggesting deaths from these hypertensive disorders of pregnancy are highly preventable. Life-threatening heavy bleeding, or hemorrhage, is also one of the major risk factors for death and is easily preventable. One way this can be done is to develop checklists that document bleeding over time and interventions to address it; these checklists must be accessible to all members of a health care team.

Causes of Pregnancy-Related Death in the U.S.

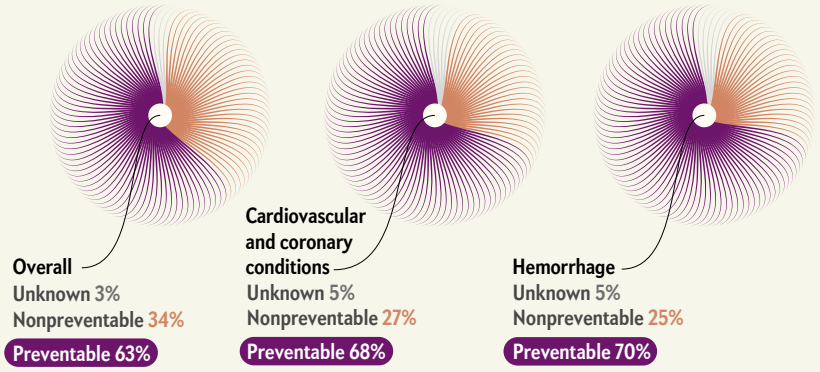
1987–1990 and 2006–2010



There have been significant reductions in pregnancy-related deaths in hypertensive disorders and hemorrhage. MMR rates are dynamic and shift over time.

Distribution of Preventability among Pregnancy-Related Deaths

Per a 2018 report including data from nine states, spanning 2008–2017



About a third of all maternal deaths are considered to be nonpreventable. But the most common conditions associated with maternal mortality, such as heart disease and hemorrhage, can be better handled to avoid poor outcomes.

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How the U.S. Is Tackling the Problem—Or Not

Recently several groups, including the World Health Organization, have called for a more respectful approach to maternal care. This would be helped by diversification of the health care workforce so that clinical teams reflect the populations they serve. It also means better communication of knowledge between patients and their health care teams. One program that embraces these features is called the Alliance for Innovation on Maternal Health (AIM). Funded through the federal Maternal and Child Health Bureau, AIM is a national alliance to promote consistent and safe maternity care, with the initial goal of reducing maternal mortality by 1,000 instances—and severe maternal morbidity by 100,000 instances—between 2014 and 2018. Many states are currently participating. The efforts involved in AIM include hospital-based interventions whereby health care teams—from obstetricians to emergency room staff—practice simulations of emergencies. The alliance also advocates for increased access to doulas and midwives, as well as a reclamation of normal physiological birth—that is, not treating birth as a disease to be managed.

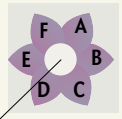
Which States Are Taking Action?

Alliance for Innovation on Maternal Health

KEY

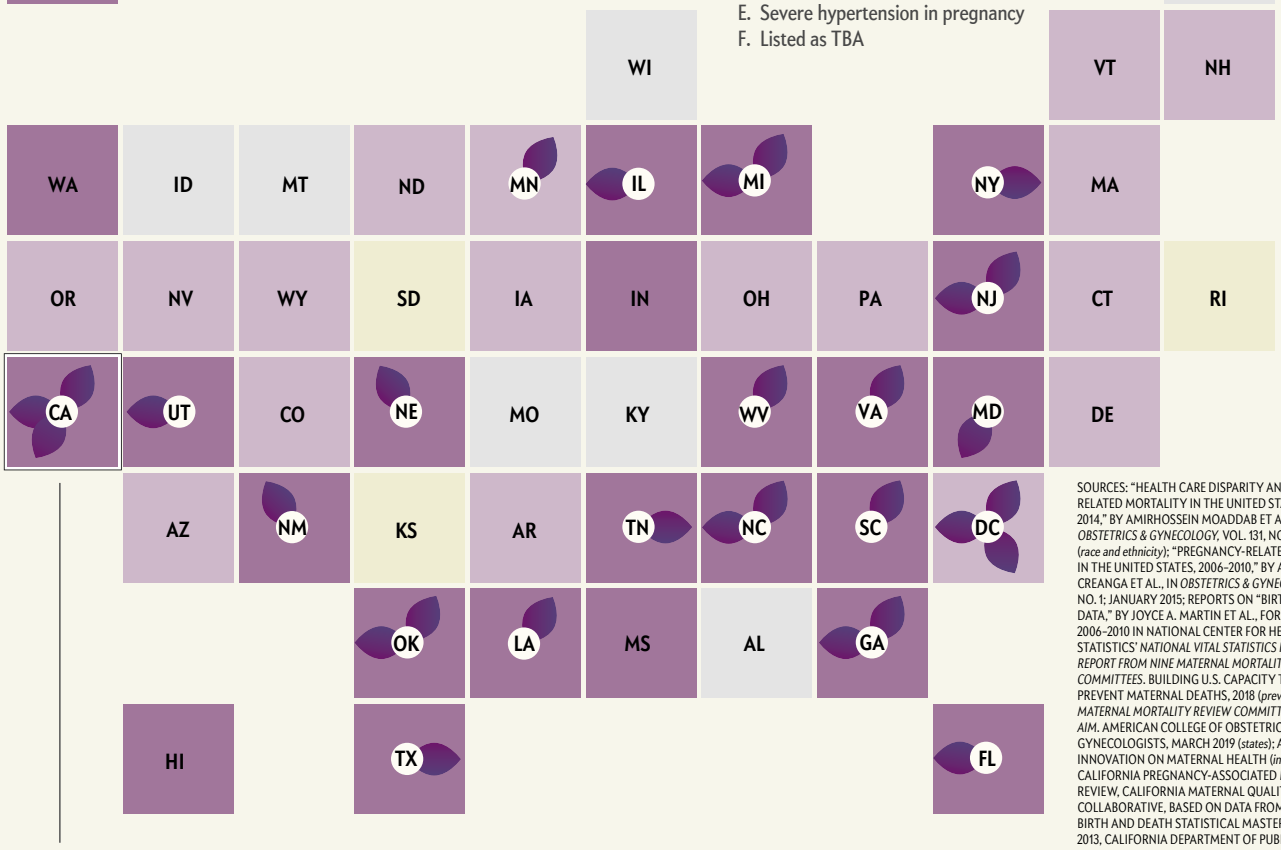
AIM states as of May 2019

- AIM states
- States with intent to apply
- States exploring engagement
- No data



AIM initiatives in place as of May 2019

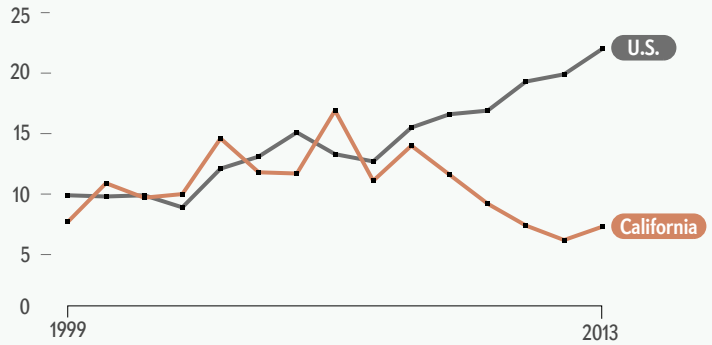
A. Obstetric hemorrhage
B. Obstetric care for women with opioid use disorder
C. Reduction of peripartum racial/ethnic disparities
D. Safe reduction of primary cesarean birth
E. Severe hypertension in pregnancy
F. Listed as TBA



SOURCES: "HEALTH CARE DISPARITY AND PREGNANCY-RELATED MORTALITY IN THE UNITED STATES, 2005–2014," BY AMIRHOSSEIN MOADDAB ET AL., IN *OBSTETRICS & GYNECOLOGY*, VOL. 131, NO. 4; APRIL 2018 (*race and ethnicity*); "PREGNANCY-RELATED MORTALITY IN THE UNITED STATES, 2006–2010," BY ANDREEA A. CREANGA ET AL., IN *OBSTETRICS & GYNECOLOGY*, VOL. 12, NO. 1; JANUARY 2015; REPORTS ON "BIRTHS: FINAL DATA," BY JOYCE A. MARTIN ET AL., FOR THE YEARS 2006–2010 IN NATIONAL CENTER FOR HEALTH STATISTICS' *NATIONAL VITAL STATISTICS REPORTS* (*age*); *REPORT FROM NINE MATERNAL MORTALITY REVIEW COMMITTEES*. BUILDING U.S. CAPACITY TO REVIEW AND PREVENT MATERNAL DEATHS, 2018 (*preventability*); *STATE MATERNAL MORTALITY REVIEW COMMITTEES, PQCS, AND AIM*. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, MARCH 2019 (*states*); ALLIANCE FOR INNOVATION ON MATERNAL HEALTH (*initiatives*); CALIFORNIA PREGNANCY-ASSOCIATED MORTALITY REVIEW, CALIFORNIA MATERNAL QUALITY CARE COLLABORATIVE, BASED ON DATA FROM CALIFORNIA BIRTH AND DEATH STATISTICAL MASTER FILES, 1999–2013, CALIFORNIA DEPARTMENT OF PUBLIC HEALTH (*California vs. U.S. MMR*)

California vs. U.S. Maternal Mortality Rate

Maternal deaths per 100,000 live births (1999–2013)



California Leads the Way

Established in 2006, the California Maternal Quality Care Collaborative (CMQCC) has used data-driven approaches in an attempt to understand the root causes of maternal mortality. A few of their tactics include distributing plain-language tool kits, conducting mock emergencies, making quality improvements in hospital settings and training staff to work more collaboratively. So far the program has reduced the MMR from 16.9 per 100,000 people to 7.3. In addition to tapping into the latest research at its Maternal Data Center, the CMQCC does outreach partnerships to improve health outcomes for mothers and infants. Parsing its successes more closely has shown that much work still needs to be done. Despite admirable reductions in overall maternal mortality in California, significant racial disparities remain and align with the demographics represented in the national data sets. Keeping black women alive before, during and after birth is the focus of an innovative new CMQCC program—a hospital-based racial equity pilot. In several communities, organizations led by black women are working with CMQCC to redesign obstetric practices. Data from the pilot should be available in 2020.

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Eggs on Ice

Technical advances are driving a boom in egg freezing, which promises to let women put off pregnancy. But will the science live up to the hype?

By Liza Mundy

Photographs by Jamie Chung

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EQUIPMENT for in vitro fertilization includes syringes for injectable medications, petri dishes, sperm vials, and more.

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SPRIGHTLY YELLOW SEEMS TO BE THE HUE OF CHOICE FOR CORPORATE WELLness chains designing a logo to attract health-minded women. There is the cleansing grapefruit of SoulCycle, the happy buttercup of Drybar. And in 2018 vans started materializing at busy pedestrian spots in Manhattan and Los Angeles that sported the shade of sunflowers. These vans are mobile fertility clinics, inviting women to pop in and learn how to safeguard their reproductive germ line by freezing their eggs. "Own your future," the ads on the side promise. "Your fertility, understood."

The vehicles are emissaries of Kindbody, a boutique fertility practice that courts the same clientele that frequents spin classes and blow-dry bars. It is one of a small but growing number of outfits that offer fertility services, including retrieving a woman's eggs, or oocytes, to be frozen for later use. Because eggs are one of the most important factors in female fertility, and both their quality and quantity decline with age, banking eggs promises to lengthen a woman's window of fertility and postpone the decision of whether to have kids. As a rival service, Extend Fertility, puts it, "Women have more options today than ever before. And we're giving you one more—the option to start your family when you're ready."

The appearance of boutique egg-freezing outfits is one of the most high-profile—but not the only—recent developments in assisted reproductive technology, which is the science (and commerce) of helping people have the babies they want. These stand-alone clinics exist thanks to a convergence of female financial empowerment, venture capital backing and real medical progress. And it is not just mobile clinics behind the push. Egg freezing is on the rise at gold-standard fertility clinics, such as the one at the University of Southern California. There, according to clinic director Richard Paulson, it accounts for almost 40 percent of egg-retrieval cycles—in which women inject themselves with hormones to stimulate their ovaries to release multiple eggs, and doctors then collect those eggs while the women are under anesthesia. (The other 60 percent of cycles at the clinic involve women undergoing infertility treatment who intend to use the eggs soon.)

Ultimately these providers are making the case that egg freezing has come far enough to justify the $10,000-plus bet women place by investing in the procedure and medications not covered by insurance (that price tag does not include the storage fees women must pay yearly to keep the eggs on ice). This confidence stems from significant breakthroughs in the science of fertility and conception made over the past decade, notably a process that allows doctors to flash-freeze eggs. Physicians have also come a long way in the science of in vitro fertilization (IVF)—the process that comes after egg freezing—which unites a thawed egg (or a fresh one) with a sperm for conception in a petri dish and then grows the resulting embryo to the point where it can be put back inside a woman's uterus to implant.

All this amounts to a sea change in the science of making babies, one that suggests, in theory, that women are not bound by the traditional notion of the ticking biological clock. Yet in practice, the reality is more complicated. Women must consider other factors besides their eggs, such as their overall health and the health of the sperm they plan to use, in deciding when to get pregnant. And just how good of a bet these new technologies truly are remains to be determined: the vast majority of frozen eggs at clinics have yet to be thawed. The question persists: Will they all be viable? Can science really safeguard fertility for later?

THE FREEZING BOOM

IN SOME PLACES, such as the San Francisco Bay Area, the rise in egg freezing is linked in part to nearby tech companies such as Facebook and Google, which now (and with some fanfare) cover the procedure for employees. In Silicon Valley, egg freezing has become part of the benefits package a prudent career woman may consider availing herself of, a kind of 401(k) for future family formation. The boom also stems from other converging trends. One is the millennial generation's comfort with social media; boutique clinics have strong presences on Instagram and Twitter, as do a growing number of traditional clinics. Even online dating—which has sold the hope that much messiness of the human heart can be solved by downloading an app—has an impact. "Women have said to me, instead of looking at every date as 'Is this someone I could marry?' they can set that aside," says Marcelle Cedars, director of the University of California, San Francisco's Center for Reproductive Health.

The rise in freezing also bespeaks a public inured to paying a monthly fee for products. What egg freezing is—among other things—is one more paid-subscription service, like Netflix or Zipcar. Oocytes, once frozen, must be

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VITRIFICATION devices such as the S-Cryolock (*shown*) help to freeze eggs and embryos almost instantly to prevent damage.

kept frozen until used. After a woman goes through the not easy or cheap process of having eggs retrieved, she will be powerfully motivated to continue paying the storage fee, which can be as much as $500 or $1,000 a year. Every batch of eggs in liquid nitrogen represents an income stream for years, for the clinic and its investors.

But the freezing trend is also the outcome of science. Asked to reflect on stages of progress in the field, Paulson casts his mind back to when in vitro was in its infancy. The first IVF baby was Louise Brown, born in 1978, now a mother herself. The technology for the scheme was nonexistent to the point where doctors had to fashion their own utensils to retrieve eggs and incubate embryos; when the late gynecologist Patrick Steptoe and the late physiologist Robert Edwards were performing the experiments that would result in Brown's birth, they kept embryos warm in a pouch created in the skin of a living rabbit.

Into the 1980s IVF patients could expect, at best, a 10 to 15 percent delivery rate. "We were able to help a handful of people," says Alan Penzias, an associate professor at Harvard Medical School and a doctor at Boston IVF. "But not the majority. Most people failed."

The retrieval of eggs—the well-protected female germ line—has always been hard. The 1980s saw basic techniques developed and refined; at first, doctors had to perform laparoscopic surgery to extract a single egg the instant it was ovulated. They learned to administer hormones that could cause eggs to ovulate in greater quantity and at a more predictable time and to retrieve

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INSTEAD OF growing embryos in incubators in the lab, the INVOcell device can be inserted into a patient's vagina to incubate them there.

them vaginally, with a needle that pokes through to the ovaries. The 1990s were—unexpectedly—the decade of the man. Male-factor infertility—slow or misshapen sperm or low sperm count—is a common reason couples may be unable to conceive. For a long time the only "cure" for male-factor infertility was sperm donation. Then, in 1992, scientists in Belgium announced the first live birth after using ICSI—intracytoplasmic sperm injection—in which a single sperm is injected into the egg. ICSI was a disruptive technology that cured male-factor infertility, for couples who can afford it.

For more than half a century it has been almost ridiculously easy to freeze sperm, which are stripped-down DNA missiles. The first reported human birth from frozen sperm occurred back in 1953. Not so for the egg, which is among the largest cells in the body and difficult to freeze well. Eggs are mostly water, meaning ice crystals can form, with sharp edges that damage organelles and other delicate structures. For years freezing an egg entailed dehydrating it to the fullest extent possible, then introducing tiny amounts of cryoprotectant, a kind of antifreeze that aims to prevent crystals from forming. Everything was done very slowly. "It would be this painful process that would take about two to three hours," says Amy Sparks, an embryologist at the University of Iowa, who remembers the agony of ratcheting down the temperature bit by bit. This technology enabled the first human birth from a frozen embryo in 1984; the first birth from a frozen oocyte was reported two years later, in 1986. But for eggs, freezing remained both difficult and damaging: the upshot often was like what happens when you thaw ice cream and refreeze it: icy granulation. "When it thaws, all of a sudden the water from those crystals has nowhere to go and causes damage to the cell," Sparks says.

Then, about 10 years ago, came the most important recent scientific breakthrough in assisted reproductive technology. Vitrification—from *vitrum,* Latin for "glass"—is the ability to freeze eggs (and embryos) breathtakingly fast. The procedure involves larger quantities of cryoprotectant than earlier methods and a direct plunge into liquid nitrogen, which triggers "ultrarapid cooling," minimizes the formation of ice crystals and almost instantly transforms the egg into a glasslike state. "In the past 10 years the impact of vitrification has really transformed the field in ways that we could not have foreseen," says Serena Chen, director of the clinic at Saint Barnabas Medical Center in New Jersey.

Vitrification is akin to pushing the "pause" button, Chen says; when the time comes, the laboratory pushes "play" and commences rapid thawing. The results are so showstopping that in 2018, the ethics committee of the American Society for Reproductive Medicine (ASRM)—which up to that point had declined to recommend social use of the technology—issued a paper saying egg freezing "for women attempting to safeguard their reproductive potential for the future" could now be considered "ethically permissible." In short: egg freezing has gone mainstream. Clinics disagree over whether frozen eggs are as viable as fresh, but most experts, including Paulson and Sparks, say they are very, very close. And there is no question that eggs frozen when a woman is 32 are better than fresh eggs retrieved from the same woman at 42.

But even great eggs, just like sex, do not always make a baby. Cedars explains to patients that they should not wait to use frozen eggs until their early 40s, because if they do not work, the old-fashioned method might not either. Yet here lies a quandary—if women cannot wait until their fresh eggs have declined, what is the point of freezing in the first place?

IVF STRIDES

VITRIFICATION is not the only advance helping to buoy the promise of egg freezing. Other elements of IVF have seen major improvements, such as the new standard of growing an embryo for five days in the lab before transferring it back to a woman. A decade ago embryos were often transferred at the three-day stage, when they consisted of just eight cells. Human embryos now arrive in the uterus as "blastocysts," with roughly 100 cells, which are more mature and robust and have a much greater chance of success. According to CDC data from 2016, for women younger than 35, nearly 50 percent of fresh embryos transferred at day five resulted in a live birth as compared with 34.4 percent of embryos transferred at day three. For women between 35 and 37, the percentages were 42.1 for day five versus 28.6 for day three.

Success rates are also getting better because labs can now closely replicate the chemical environment of the fallopian tube, where embryos spend their first five or so days when pregnancy happens naturally. Labs have gotten much better at regulating the amounts and concentrations of nitrogen, oxygen and carbon dioxide.

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Current incubators also feature more solid-state technology that requires less opening and closing of doors so that embryos can rest undisturbed.

The ability to develop embryos to the blastocyst stage means embryologists can more easily recognize the best of the batch before deciding which to try to implant. These judgment calls are also improved by a process called preimplantation genetic selection. Back in the three-day-embryo era, if scientists wanted to gauge the genetic health of an embryo, they had to pry one cell from an eight-cell mass, a lab procedure so harrowing that Sparks still has "nightmares" about it. Now it is much easier to use lasers to grab a couple of cells from the part of the blastocyst that will create the placenta—the less vital section than the one that is destined for the fetus.

All in all, embryologists' improved ability to freeze and test embryos amounts to "a huge change," Penzias says. About 10 years ago, frozen embryos had a 10 percent lower success rate than fresh. "Now we're talking about parity," he says. The improved odds mean, in theory, that whether women are using embryos created from eggs retrieved the same month or from those frozen years before, clinics can transfer just one embryo at a time rather than the two or three that used to be the norm. For well over a decade it has been the University of Iowa's policy that if a woman is younger than 38, has no prior failed transfers at the clinic and has at least a single good-looking blastocyst (a five-day-old embryo), then one is "all they get," Sparks says. These trends have reduced the prevalence of twins and, especially, of triplets and higher-order multiples, which are much riskier pregnancies than carrying singletons, for both babies and moms. At the University of Iowa, the rate of twin birth used to be 40 percent in 2001; now it is under 5 percent. Industry-wide, according to the CDC, the portion of transfers involving a single embryo has more than tripled, from 12 percent in 2007 to 40 percent in 2016. Equally important: the percentage of fresh single-embryo transfers resulting in a live birth increased from 21 percent in 2007 to 37 percent in 2016.

These innovations are just the beginning. A new invention allows a woman to incubate embryos inside a device inserted in her vagina rather than an incubator in the lab. And even more radical technologies are on the horizon: Mitochondrial replacement therapy, for instance, is a controversial procedure that can eliminate the risk of genetic mitochondrial disease by injecting the nucleus of a mother's egg into an egg from a woman without the disease whose nucleus has been removed but whose mitochondria remain. The procedure is banned in the U.S., out of concerns about mixing the DNA of two women, but is being developed in England. The day is also coming, Paulson says, when it will be possible to use stem cell technology to manufacture sperm and eggs from normal body cells, such as skin cells. Although it sounds like science fiction, the procedure would involve no changes to a cell's DNA, so that part, at least, is less worrisome than mitochondrial transfer. With this technology, women would no longer need to bank eggs. "At 45, you can still have an egg made out of your skin cells," Paulson says. It sounds wild, but so did IVF 40 years ago. "It's going to happen."

TICKING CLOCKS

IT IS A FACT THAT a woman is born with all the oocytes she will have; over time her ovarian reserve diminishes, as does the quality of her eggs.

Talking about this subject has always been fraught. Back in 2001, when the ASRM launched an ad campaign partly about age-related infertility, the National Organization for Women attacked it as coercive and antifeminist. Chen says this reaction does women a major disservice; older eggs are more likely to be chromosomally abnormal, with a higher risk for miscarriage and the grief that follows. She adds that egg freezing is often depicted as elective and narcissistic, "kind of like plastic surgery or getting a cute Mini Cooper." But women face many pressures, particularly in their mid-30s, when each year of delayed childbearing means an increase in earning power. "It's not about women just being selfish and trying to work on their careers," Chen says. "The truth is, a lot of people just haven't found the right partner."

Still, Chen shares concerns about the commercialization of a technology that originally aimed to help cancer patients preserve fertility during treatment. Jake Anderson-Bialis, co-founder of the consumer education Web site FertilityIQ, worries that women do not realize taking hormones and then undergoing retrieval is not a minor lunch-hour-type procedure. And there is still no guarantee the eggs will result in a live birth. The backlash could be huge if many of the women now freezing their eggs later attempt to use them, only to find out their investment failed. The dirty secret of the fertility industry, up to now, has been multiple births; going forward, Anderson-Bialis says, "if there's going to be a black eye, it's egg freezing." By this, he means the danger that the eggs, once thawed, will not be viable—a potentially devastating outcome to women sold on the promise of egg freezing. Cedars agrees that some women are too bullish on what technology can accomplish. "We have to repeatedly say to patients, 'There's not a baby in the freezer,'" she says. "'There is the *potential* for a baby.'" SA

Liza Mundy is a journalist, a senior fellow at the New America foundation and a former staff writer for the *Washington Post*. She is author of four books, most recently the *New York Times* best seller *Code Girls: The Untold Story of the American Women Code Breakers of World War II* (Hachette Books, 2017).

MORE TO EXPLORE

Mature Oocyte Cryopreservation: A Guideline. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology in *Fertility and Sterility*, Vol. 99, No. 1, pages 37–43; January 2013.

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A PAINFUL MYSTERY

Endometriosis spreads like a vine through the bodies of roughly 176 million women worldwide, causing agony and infertility. Science has struggled to understand the condition, but new research is sparking hope for improved treatments soon

By Jena Pincott

Illustration by Katherine Streeter

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EVERY WOMAN WITH ENDOMETRIOSIS

has an origin story, a memory of the first time she knew the pain in her pelvis could not be normal. For Emma, it goes back to the day in 10th-grade history class when she blacked out. The sensation, she says, was how a pumpkin might feel when its insides are scraped. Her gynecologist assumed she was having bad period cramps and gave her birth-control pills. They helped but not enough. "He made me feel as if I were acting a little crazy," says Emma, now in her late 30s, who asked to go by a pseudonym. "It struck me much later that when a woman's medical problem isn't clear-cut, she just isn't believed."

Not until about six years after the blackout did she find a doctor who recommended laparoscopic surgery of her abdomen to look for the cause of the pain. That is when she learned she had endometriosis, a disorder in which tissue normally found in the uterine lining, called the endometrium, escapes and takes root in other parts of the body. By then, the disease had carpeted her pelvic organs like kudzu.

In describing endometriosis, ecological comparisons seem apt. Just as the creeping kudzu vine wraps itself around trees and shrubs, smothering anything in its path, so, too, do adhesions (scar tissue) that form when wayward endometrial cells land where they are not supposed to. These adhesions can engulf or bind the bladder, the intestines, the ureter tubes leading to the kidneys and other pelvic organs. Lesions that are surgically removed often grow back: more than half of women who have them cut out return for another operation within seven years. When surgeons go in, they might see the bowels, ovaries and sciatic nerve bound in a macramé of scar tissue or a fallopian tube squeezed so tightly that an egg cannot pass through.

Despite the manifest damage it can cause, endometriosis is a mystery. Doctors know that it runs in families and is linked with several genetic variants—heritability hovers around 50 percent—but genes cannot yet explain its occurrence or predict its path. The degree of scarring and the number and location of lesions have little to do with the severity of the symptoms, which, besides pain, can include heavy bleeding, discomfort during sex and bowel movements, and often devastating infertility. Some patients find relief in surgery and drugs, whereas others, even with few lesions, try every known remedy and still live in constant pain.

For decades endometriosis has been ignored, and research into it has been underfunded. Endometrial pain and other symptoms reduce women's productivity at work by nearly 11 hours a week—27 percent of a 40-hour work week—according to results released in 2011 from the Global Study of Women's Health, which surveyed more than 1,400 women in 10 countries.

Finally, patient advocacy, social media activism and women-led movements for social change have brought attention to the problem, and the medical community has begun to reckon with its history of underestimating and undertreating women's health issues. Researchers are developing tools to study the complicated origins of endometriosis, to diagnose it and to design targeted treatments. Yet even at a time when women are raising their voices for better care, too many remain undiagnosed and in pain.

THE INVASION CONUNDRUM

"FIRST, HOW DOES THE TISSUE get outside the uterus?" asks Linda G. Griffith, a professor of biological and mechanical engineering at the Massachusetts Institute of Technology. As scientific director of the M.I.T. Center for Gynepathology Research and an endometriosis patient herself, she is deeply vested in the question, which has perplexed her fellow scientists for decades. No one knows for certain how or why endometrial cells show up outside the endometrium.

The prevailing theory, called retrograde menstruation, was proposed nearly a century ago. John Sampson, a gynecologist, observed that menstrual fluid containing cells from the uterus can flow backward up the fallopian tubes. Bits of that fluid, he suggested, stick to pelvic organs and the abdominal lining or float in pelvic fluid and spread to distant sites. It happens to just about every woman and is normally cleared by the immune system. But sometimes, Sampson's theory goes, the cells implant wherever they land. The misplaced tissue acts as if it is still in the uterus: it sprouts hormone receptors and responds to hormonal signals. Every month it grows as the uterine lining grows, secreting hor-

IN BRIEF

Endometriosis afflicts approximately 10 percent of women worldwide, yet it continues to present a medical mystery.
Scientists do not understand why the cells lining the uterus sometimes grow in other places in the body, triggering extreme pain, inflammation and scar tissue.
The disorder has long been dismissed and underfunded, but endometriosis is gaining visibility.
Research is picking up, with one lab developing a diagnostic test that detects certain miRNAs that appear more frequently with the syndrome.

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mones, and sheds when the cycle ends. But unlike a period, the blood and tissue get trapped in the pelvis and trigger inflammation. Over time the inflammation leads to scarring and adhesions.

Ever since Sampson, researchers have been divided about the underlying cause of the disease. Is the defect in the "seed," the rogue endometrial cells, or is it in the "soil," the abdominal environment where those cells implant and spread? Theories on the seed side blame defective endometrial cells or stem cells. The soil side claims that endometriosis is primarily an immune dysfunction. A third theory splits the difference, saying, essentially, that the soil changes the seed. "Women with endometriosis may have had normal endometrial cells until the lesions took root and created changes in the tissue," Griffith explains, suggesting that the immune response to the lesions is the likely driver. The resulting inflammation may alter the expression of progesterone and estrogen receptors in endometrial cells: as a result, cells pump out more estradiol, a form of estrogen that fuels growth of lesions, unchecked by progesterone. In a baboon experiment in 2006, researchers were able to induce endometriosis by injecting normal uterine lining into the pelvic cavity.

Kevin G. Osteen, a professor of obstetrics and gynecology at Vanderbilt University, has proposed that environmental toxins play a role, at least in some cases. His research focuses on one of the most toxic of environmental pollutants, the industrial byproduct dioxin, and dioxinlike chemicals called polychlorinated biphenyls (PCBs), which are found in meat, fish, dairy products and, in varying amounts, all our bodies. Osteen's theory is that exposure to these toxins in utero disrupts the physiology of the developing endometrium. When he and his colleagues exposed human endometrial tissue to dioxin in a series of experiments, the tissue became resistant to progesterone and prone to inflammation. Without progesterone to tamp down enzymes known as matrix metalloproteinases, which regulate the monthly rebuilding of the uterine lining, endometrial tissue may become invasive, spreading beyond its normal domain in the uterus.

Griffith suspects that whatever caused her endometriosis, it happened early in life. Retrograde menstruation may apply to many cases, she says, but probably not hers. She developed harrowing symptoms from day one of her first period, long before lesions from menstruation had time to develop. Some researchers argue that patients in this category may have had a retrograde flow of endometrial cells during the normal vaginal bleeding that often occurs shortly after birth in female infants. Or when baby girls are still in the womb, endometrial-like cells or stem cells could have landed outside the uterus, sometimes as far afield as the lungs and brain (evidence of these wandering cells has been found in miscarried and aborted fetuses). "Those cells could sit there until the girl starts going through puberty," Griffith explains—like ticking time bombs.

Similar to cancer, endometriosis has many causes and manifestations. As Griffith puts it, "It's likely not one disease but many."

AN ECOSYSTEM OF PAIN

WHEN WOMEN TALK about endometriosis, they talk about pain. They talk about the sick days from school or work, lost time and opportunities, the diminishment of life's pleasures. They talk about arranging their calendar around their period or a night on morphine in the ER. One of the hardest things for them to hear is that the pain is "all in their head."

Female suffering has a history of being downplayed by the medical establishment. In 2008 a study in the journal *Academic Emergency Medicine* found that women wait longer than men in emergency rooms before receiving treatment for the same abdominal pain, and they are 13 to 25 percent less likely than their male counterparts to receive opioid painkillers (after controlling for age, race, triage class and pain score). An earlier study of cardiac patients found that nurses were likelier to administer painkillers to men and to give women sedatives. And even when women do get painkillers, the medication may be less safe and effective for them because many pain studies have been conducted on men or male mice.

Even after finally getting a diagnosis, Emma lost an ovary to endometriosis when she was 26. A decade later she gave birth to a daughter and is now relatively pain-free but not without regret about the years she spent misdiagnosed and undertreated. "If I could redo my life," she says, "I'd have pushed for answers sooner." She did not know that endometriosis even existed when her pain first started. Nor, it seemed, did her doctors, she says.

One reason doctors and even patients minimize pain caused by endometriosis is that it flares up during menstruation when women are "supposed" to feel bad. "Pain is very subjective. Cramps are the only pain that is considered 'normal,' and it's hard to know when that pain is abnormal," explains Hugh S. Taylor, chair of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine. Taylor adds that social norms have prevented open conversation about menstrual pain, pain during sex or pain with bowel movements—all red flags of endometriosis. "Fortunately," he says, "these barriers are decreasing," and doctors, as well as patients, increasingly feel comfortable bringing these topics up and investigating their causes.

And patients can play a more active role in the fight against endometriosis. For instance, they can participate in research through the "citizen scientist" app Phendo, launched in 2016 by biomedical informatics scientists at Columbia University. Users track and identify their patterns and triggers, and the data will be used to study the disease's causes and to design treatments.

"For decades endometriosis advocates have been cultivating communities that empower, inform and educate patients," says Casey Berna, a patient advocate and organizer. "Now there is a movement to reject historically paternalistic approaches to care and to include the patient voice, especially when managing complex diseases."

In April 2018 Berna and her colleagues organized a protest by patients outside the Washington, D.C., headquarters of the American College of Obstetricians and Gynecologists (ACOG), demanding its member doctors be better trained to diagnose endometriosis and to get patients the best and latest treatments—to stop, for instance, prescribing needless hysterectomies. "To put it plainly," Berna says, "the current standards are responsible for decades of suffering endured by millions of patients. We're calling on the ACOG to work with patient advocates and endometriosis experts to utilize all of their resources to address this crisis of care."

Experts agree that too many physicians still miss the disorder. "Pediatricians and most primary care doctors are [still] not well educated about endometriosis," Taylor says. And when endometriosis goes undiagnosed, it often worsens. "Misplaced endometrial tissue has higher than usual levels of aromatase, an enzyme that makes the lesions estrogen-dominant, which in turn drives

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their growth," explains Pamela Stratton, a gynecologist and surgeon at the National Institutes of Health. The lesions also become resistant to progesterone, which would otherwise help curb endometrial growth and fight inflammation. As a result, inflammation reigns: prostaglandins (lipids that form more quickly when tissue is damaged) and pro-inflammatory proteins called cytokines act on nerve endings and ratchet up pain sensitivity. Over time adhesions form and interfere with the function of pelvic organs, causing more pain.

One of the strange features of endometriosis pain is that it bears little relation to the severity or location of the lesions. A woman with few lesions may feel as if her pelvic organs are being pulverized in a meat grinder, whereas a serious "stage IV" patient with lumps that protrude from her belly may be pain-free. Doctors may overlook adenomyosis, which occurs when endometrial tissue invades the muscle wall of the uterus; lesions here are difficult to see during surgery, but the patient is in eye-popping agony. For many women pain persists even after lesions have receded or are surgically removed.

At this point, the problem is not just in the pelvis anymore, Stratton explains; now it is a central nervous system disorder. All too often with endometriosis, the brain has been tuned in to pain for so long that it cannot turn off, even after the pain trigger is gone. In this condition, called central sensitization, neural wiring has effectively remodeled itself to be "alert to hurt." Any minor disturbance, including ovulation, menstruation and sex, triggers and perpetuates the pain. Genetics may play a role, Stratton notes, but the details are not well understood. Women with few or tiny lesions can still suffer debilitating chronic pain, leading to central sensitization, she says. A troubling irony is that these women may be the most likely to have a doctor tell them there is nothing wrong because many gynecologists are unaware of the possibility of central sensitization. "Because they are not neuroscientists," Stratton says, "they don't consider what neuroscientists have learned about pain."

Stratton, who straddles both worlds, is exploring treatments to address pain and perhaps reverse central sensitization in endometriosis patients. If a drug can relieve pain for an extended period, she posits, the central nervous system may be able to reset its pain threshold. Stratton is conducting a clinical trial of botulinum toxin, commonly known as Botox. Injected in the pelvic floor, it relaxes muscle spasms and may alter the chemicals involved in pain signaling. Although the full study will not be complete until 2020, she says, her group released a proof-of-concept study with promising results: 11 of 13 patients reported pain as mild or nonexistent within two months postinjection; for seven, relief lasted five to 11 months.

The stakes are high. Chronic pain causes sleeplessness, anxiety, depression, irritability and brain fog. Several neuroimaging studies have found alterations in the gray matter of chronic pain patients, including loss of volume in the hippocampus (which may explain memory impairment) and the prefrontal cortex (which may underlie deficits in pain regulation and cognitive function). A small study of endometriosis patients with chronic pelvic pain found shrinkage in the thalamus, insula and other regions associated with pain modulation. Tracking chronic back pain patients, Northwestern University researchers compared the loss in gray matter volume—1.3 cubic centimeters every year—with the effects of 10 to 20 years of normal aging.

Invasion of Pain

Endometriosis is an agonizing disorder that affects about 10 percent of women worldwide yet largely baffles scientists. It occurs when endometrial cells, which normally line the walls of the uterus, escape and grow elsewhere, prompting inflammation and scar tissue.

RETROGRADE MENSTRUATION

A leading theory suggests that endometriosis occurs when menstrual fluid during a woman's period flows backward through the fallopian tubes into a woman's abdomen. Wherever it lands, the endometrium continues to grow and shed with the woman's cycle, and the trapped blood and tissue lead to scarring and inflammation.

Illustrations by David Cheney

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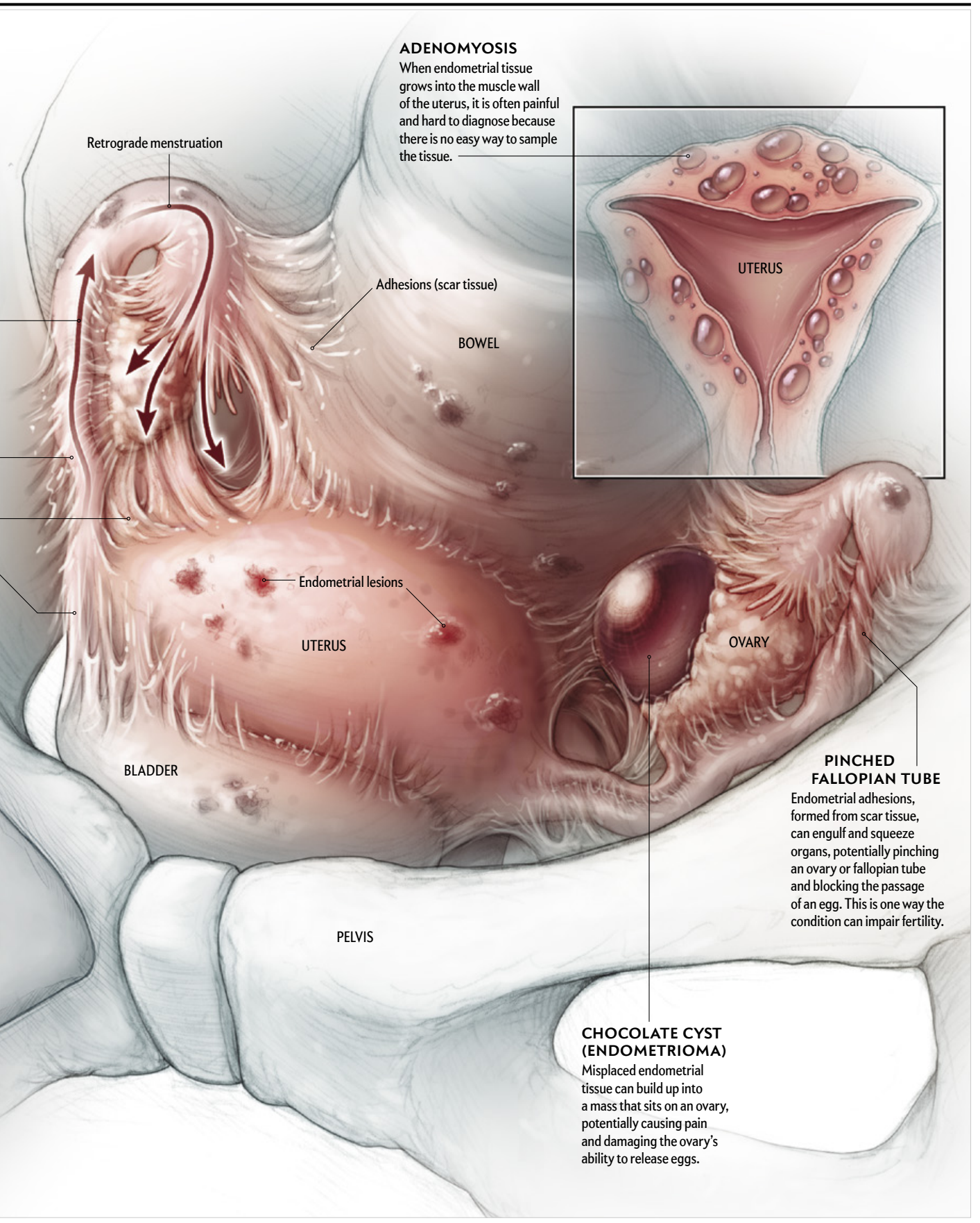
ADENOMYOSIS
When endometrial tissue grows into the muscle wall of the uterus, it is often painful and hard to diagnose because there is no easy way to sample the tissue.
Retrograde menstruation
Adhesions (scar tissue)
BOWEL
UTERUS
Endometrial lesions
UTERUS
OVARY
BLADDER
PELVIS
PINCHED FALLOPIAN TUBE
Endometrial adhesions, formed from scar tissue, can engulf and squeeze organs, potentially pinching an ovary or fallopian tube and blocking the passage of an egg. This is one way the condition can impair fertility.
CHOCOLATE CYST (ENDOMETRIOMA)
Misplaced endometrial tissue can build up into a mass that sits on an ovary, potentially causing pain and damaging the ovary's ability to release eggs.

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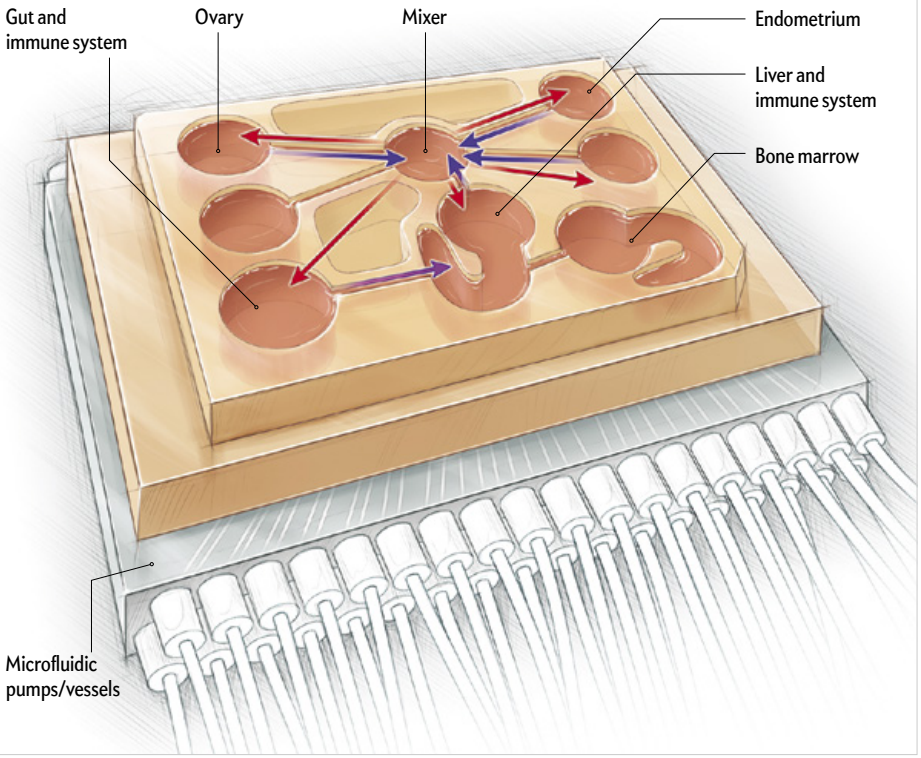
Organs on a Chip

Scientists are designing microscale versions of body organs to test drugs to treat endometriosis. These so-called organs-on-a-chip avatars contain real living cells that scientists can expose to hormones, pharmaceuticals and other cues. Each platform contains a set of mini organs important for disease processes, plus a mixing chamber, or "mixer," to simulate systemic circulation. For example, the uterine lining (endometrium) and ovary here are connected to gut, liver and bone marrow, which are involved in drug metabolism and immune response. This PhysioMimetics platform is being developed at the Massachusetts Institute of Technology.



A BLIGHT ON FERTILITY

WHEN WOMEN WITH ENDOMETRIOSIS talk about their fears, infertility ranks high. About half of women with infertility have endometriosis. In a cruel trick of nature for those who struggle to conceive, endometriosis pain is said to feel like labor pain. A blockage of the fallopian tube can avert the passage of the egg from the ovary to the uterus, and inflammation from scarring or surgery around the ovaries can compromise egg follicle quality and quantity. Pro-inflammatory cytokines and other elements in the peritoneal fluid surrounding the pelvic organs can reduce sperm motility in the fallopian tubes and damage eggs and embryos. Problems can arise in the hormones, too. Conception is a hormonal and immunological symphony; in endometriosis, the conductor has left the room. Normally after ovulation, the concentration of estrogen receptors in the uterine wall dwindles to prepare for implantation. Progesterone rises, cueing the endometrial lining to receive and nourish the fertilized egg. The hormone calms the uterus and prevents contractions. (The root of progesterone is "progestation.") But in endometriosis, the uterine lining is resistant to progesterone, and the competing hormone estradiol remains dominant, among other factors that make the environment less receptive to a blastocyst. Even if implantation occurs, progesterone resistance may lead to a higher risk of miscarriage and premature birth.

Adding to the complexity are clues that the endometrium has a microbiome, which also becomes disordered in endometriosis. Recent studies suggest that *Lactobacillus* bacteria dominate the uterus in most women and have a part in implantation and support of the growing embryo. The idea remains speculative, but chronic inflammation caused by endometriosis may kill off lactobacilli, creating a microbial imbalance in the uterus that perpetuates inflammation and potential infertility. In 2016 a preliminary investigation published in the *American Journal of Obstetrics & Gynecology* found that when non-*Lactobacillus* microbes dominate, as they do in endometriosis, implantation occurred at only one third the normal rate, and the number of miscarriages shot up. Although the cause of the connection is not clear, studies such as this one have inspired research into the role of the endometrial microbiome in endometriosis, and some doctors may consider testing endometrial cultures before fertility treatment.

There are success stories, too. Approximately 43 to 55 percent of endometriosis patients are able to conceive through one cycle of in vitro fertilization (IVF), depending on the stage of their disease, and women with endometriosis who do become pregnant through IVF have similar live birth rates to those without the disease. In the hormonal milieu of pregnancy, symptoms usually subside. Breastfeeding, too, is linked with a lower risk of endometriosis. This 2017 finding, derived from a data set of more than 70,000 women, showed that for every three months of exclusive breastfeeding, the risk of a woman developing endometriosis drops by 14 percent, compared with breastfeeding for less than a month. It remains an open question whether lactation-related hormones and immunological factors can relieve the symptoms of women who already have endometriosis.

BETTER TOOLS AND TREATMENTS

WHEN SCIENTISTS TALK about endometriosis, they always bring up the seven-year hitch: the average lapse between the onset of pain and a diagnosis, by which time a lot of damage may be done. A diagnosis currently requires a surgical procedure (laparoscopy), but the disease could be caught much earli-

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er if it could be identified with a simple blood, saliva or urine test. The challenge is to find the right signal to look for.

In recent years several laboratories have homed in on microRNAs (miRNAs): short, noncoding sequences of RNA that regulate gene expression and are shed by tissues. In 2016 Taylor's group identified three miRNAs that are more prevalent in endometriosis patients, compared with control subjects. Taylor's company, DotLab, will use these miRNAs as a basis for the first diagnostic saliva test for endometriosis, which Taylor says has an accuracy of well over 90 percent. The lab recently got a new round of funding, and the test, administered by prescription, is poised to launch in the near future. If it succeeds, women may receive treatment earlier, Taylor says, and doctors may also use it to discern whether a drug they prescribe is effective. After all, a diagnosis, early or not, does not ensure relief. Some drugs work at first, then lose effectiveness. Others trigger menopauselike symptoms.

In the future, a newly diagnosed patient might start her treatment with a skin biopsy, envisions Julie Kim, a professor of obstetrics and gynecology at Northwestern University. Cells gathered from a tiny skin punch in a woman's thigh or lower hip would be engineered to travel backward in developmental time to become induced pluripotent stem (iPS) cells, which can grow into any cell in the body: endometrial cells, liver cells, kidney cells, and so on. Each cell type would be used to seed a "micro organ" on a tablet-sized electric circuit that represents her body—in other words, her medical avatar.

Several organ-on-a-chip avatars are already here. The one Kim built as co-investigator resides at the Woodruff Lab at Northwestern: the EVATAR (a mash-up of "Eve" and "avatar"). It is a miniature female reproductive system, complete with micro ovaries, fallopian tube, uterus, cervix and liver. Like other patient avatar platforms, the EVATAR's "organs" are harbored in dime-sized vessels that sit on a plate connected to a computer. Artificial blood flows through minuscule channels connecting the organs, carrying hormones, nutrients, and growth and immune factors. The EVATAR has a monthly cycle but does not bleed.

A patient with an EVATAR would know which drugs are likeliest to help her; after all, every micro organ on the platform holds her specific genetic blueprint. "Say we're testing a drug designed to reduce endometrial lesions," proposes Kim, describing the kind of study she anticipates doing with the EVATAR. Her lab would expose the system to the experimental treatment. During the menstrual cycle, the scientists would collect and analyze data from each organ to see, at the cellular level, if the drug is safe and effective against that patient's lesions. This kind of experiment also avoids the problem of many drugs and treatments being tested on men and animals and then not translating to women and opens the door to custom medicine.

Kim's lab has shown a proof of concept with the EVATAR, but developing an endometriosis platform and testing drugs could take up to five years, Kim says. It may be longer before the platform can test individual patients; the time line depends on many factors involved in taking a research tool to the clinic. The project can only work, she says, "if the resources are available and there is a priority given to endometriosis research."

In Griffith's view, custom drug testing on individual patient avatars is prohibitively expensive, but organs on a chip still have a role to play in figuring endometriosis out. Instead of using an organ-on-a-chip platform for each patient, Griffith hopes to classify women with endometriosis by several molecular markers, similar to what is done for breast cancer, then develop drugs that target each type. "All patients are different," she says, "but we believe there may be groups of patients with common features."

The first step toward finding those groups, Griffith explains, is to build computer disease models and a few hypothetical classification schemes. Next, she would recruit hundreds of patients from multiple clinics and test those models on them. Griffith predicts that three to five groups will emerge that have different types of dysfunction, each with characteristic molecular signatures.

Griffith's organ-on-a-chip platform—called PhysioMimetics—can connect up to 10 mini-organ systems on an integrated circuit, including a tiny endometrium designed by Christi Cook, a former Ph.D. student in Griffith's lab. The chip endometrium consists of a polymer "hydrogel" scaffolding that supports several layers of endometrial tissue cell types. Researchers can apply various hormones and inflammatory cues to the tissues to see what happens.

Once Griffith has identified her disease-type groups—each with its own unique molecular markers—she plans to use the organ-on-a-chip platform and partner with pharmaceutical makers to test drugs that target the specific disease pathways in each group. If the drug appears to be safe and effective on the avatars, she will try it on flesh-and-blood patients.

Despite the promise of organs on a chip and other tools, however, the medical community has a long way to go to fight endometriosis effectively. Funding for research on the disorder is still incommensurate with the disease's societal costs: $62 billion annually in the U.S., including lost work productivity and direct health care costs, according to a 2012 study by the World Endometriosis Research Foundation. An NIH report shows that in the U.S., nearly $1 billion will be spent on diabetes research in 2018, compared with $7 million on endometriosis, which afflicts about the same percentage of women. "If you look in PubMed," the online archive for biomedical studies, Griffith says, "you will find more than 20,000 papers for erectile dysfunction but only about 2,000 papers on adenomyosis, which is estimated to be as common as endometriosis. Who misses work for the first one?"

Fortunately, Griffith says, talent is attracted to the field because the research is "fascinating scientifically"—and also happens to be crucial to society. After all, there is no cure yet: the closest thing is a surgical absence of disease, to which Emma would add, "And a subjective absence of pain." When chronic pain goes away, the mind heals. Gray matter can and does regrow. But like kudzu, endometriosis is tough to subdue—beating it back will take a concerted effort by researchers and doctors, as well as a real financial commitment from a society finally ready to take this disorder seriously. SA

Jena Pincott is a freelance writer who focuses on the quirky, hidden side of science. She is author of several books, including *Do Chocolate Lovers Have Sweeter Babies? The Surprising Science of Pregnancy* (Free Press, 2011). Her writing has appeared in the *Wall Street Journal*, Oprah.com, *Psychology Today* and *Nautilus*, among other publications.

MORE TO EXPLORE

Columbia University's Phendo, an app to track endometriosis: **http://citizenendo.org/phendo**
Endometriosis saliva test information from DotLab: **www.dotlab.com**

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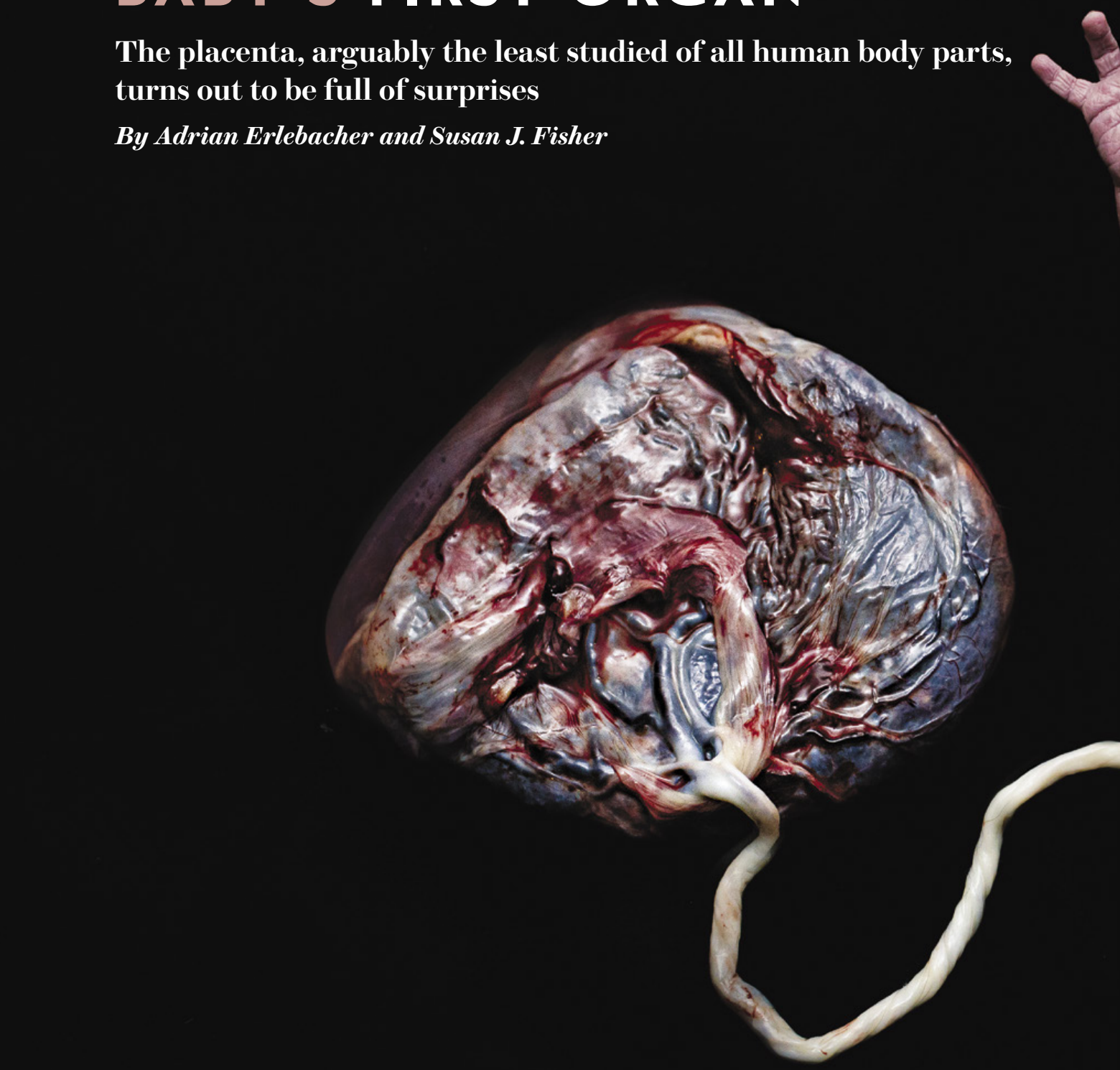
BABY'S FIRST ORGAN

The placenta, arguably the least studied of all human body parts, turns out to be full of surprises

By Adrian Erlebacher and Susan J. Fisher



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PLACENTA (*left*) is still attached to a newborn here, although it is typically delivered soon after the baby emerges and the umbilical cord is cut.

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FOR DECADES PUBLIC HEALTH OFFICIALS THOUGHT THE ZIKA VIRUS caused only relatively mild illnesses in people. Since the start of an outbreak in Brazil in 2015, however, it has become horribly clear that the virus can pass from pregnant women to their fetuses, with devastating consequences. The virus kills some of the unborn children and leaves others with severe brain damage, including smaller than normal heads (a condition called microcephaly). How the virus reaches the fetus is a mystery because to get there, it must cross the placenta, a pancake-shaped organ that connects the developing infant to the mother and that manages to block transmission of other closely related mosquito-borne viruses, such as dengue and yellow fever, from mother to baby.

In the past several years this puzzle and others have drawn new research attention to the placenta, which is the first and largest organ to develop after conception. It is a product of the embryo, not the mother, and among other things, it supplies the fetus with nutrients and oxygen and disposes of waste products. Yet despite its critical role in pregnancy, it is arguably the least understood organ in the human body.

The placenta's vulnerability to Zika is not the only conundrum. Researchers have long wondered why a mother's immune system does not recognize the placenta and the fetus as genetically foreign and therefore target them for attack. In fact, not only does the mother's immune system keep itself in check, it actually aids in the proper development and functioning of the placenta.

Research carried out by our laboratories and others has begun to yield fascinating insights into these questions. Through these findings, we are increasingly realizing that certain complications of pregnancy—once thought to be caused entirely by problems in the mother's body—are attributable to defects in the placenta or its interaction with the uterus. What is more, subtle variations in the placenta might affect a person's health later in life.

RAPID DEVELOPMENT

ALTHOUGH MYSTERIES related to the placenta abound, two aspects are well understood: the organ's structure and the basic steps of its development. At the time of delivery, the slablike placenta weighs just more than a pound and has two distinct sides: the part attached to the mother's uterine wall before delivery, which has the appearance of a blood-soaked sponge, and the one facing the baby, which contains an array of blood vessels that traverse the umbilical cord [*see box on pages 64 and 65*].

The placenta develops quickly because it has to do the jobs of other developing organs until they become fully functional—like the liver, it metabolizes nutrients; like the lungs, it exchanges oxygen for carbon dioxide; like the kidneys, it excretes wastes. Less than a week after a sperm fertilizes an egg, specialized cells called trophoblasts emerge on the surface of the embryo. The first task for these cells (which also produce hormones that alert the mother's body to the presence of the embryo) is to burrow into the uterine wall. There the trophoblasts divide rapidly, forming projections that radiate into the uterus. One layer is composed of cells known as cytotrophoblasts. Another layer of fused cells (known as syncytiotrophoblasts) becomes the surface of the placenta. Eventually the placenta takes the form of a disk

IN BRIEF

A successful pregnancy depends on the proper development and functioning of the placenta—an unusual organ that both separates and connects a pregnant woman and her fetus.
Recent studies suggest why the mother's immune system does not reject her unborn child as foreign tissue—and how certain maternal cells actually help the placenta form and infiltrate the uterus.
A better understanding of malfunctions at the maternal-fetal interface could explain dangerous complications of pregnancy, such as preterm birth, intrauterine growth restriction and preeclampsia.
Scientists are also trying to figure out how some viruses, such as Zika, are able to breach the placenta, whereas others cannot.

PRECEDING PAGES: MONET MOUTRIE

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FIVE-WEEK-OLD PLACENTA already has a branching structure but is relatively pale because it is not yet perfused by the mother's blood. This one is from an aborted pregnancy; normally at this stage it would entirely surround the embryo and its amniotic sac.

that is attached to the uterine wall by branching structures.

During the second and third weeks after fertilization, these branches begin to fill with support cells and blood vessels. By around the time a woman learns she is pregnant, the mature configuration of these structures, now known as chorionic villi, has been established.

In the placenta's race with time to become fully functional early in pregnancy, its ability to reroute maternal blood flow to itself is paramount. The extraordinary journey that cytotrophoblasts take makes this feat possible. First, the cells attach themselves to the surface of the uterine wall, then they migrate ever deeper inside. Nearly two decades ago one of us (Fisher) discovered that the cytotrophoblasts transform themselves during this process so that they mimic the cells that typically line the blood vessels. This mimicry enables the cytotrophoblasts to breach the mother's oxygen-laden arteries [*see box on next two pages*]. Once inside, they climb up each vessel's inner lining, replacing it as they go.

Because of the cells' machinations, the mother's arteries in the uterus expand and lose their normal "tone," which would otherwise restrict the amount of blood they can carry. By the end of the first trimester, the arteries open into the spaces between the chorionic villi, delivering the large quantities of maternal blood (and thus nutrients and oxygen) required for the offspring's growth. The cytotrophoblasts also invade the uterine veins, enabling blood to flow from the placenta back to the mother's body, which completes the circuit and carries carbon dioxide and other waste products away from the fetus.

Blood from the mother's arteries bathes the surface of the placenta just a few cell layers away from the offspring's own blood vessels. This proximity maximizes the exchange of nutrients, gases and waste products. Researchers have also determined in the past few years that the placenta releases large quantities of the offspring's DNA into maternal blood, which makes it possible to do prenatal genetic testing with only a blood sample from the mother. Such tests are rapidly replacing older, more invasive procedures, such as chorionic villus sampling and amniocentesis.

ENVIRONMENTAL INFLUENCES

THE GENES of the fetus direct much of the placenta's development, but the microenvironment surrounding the organ also plays a vital role. Research over the past two decades has begun to reveal how much a successful pregnancy relies on the interchange between maternal cells in the uterine tissue and the invading branches of the placenta. The areas where the placenta and uterus meet—the so-called maternal-fetal interface—harbor various kinds of immune cells called leukocytes that migrate to the site from the mother's blood. The trophoblasts from the fetus maintain an ongoing dialogue with these leukocytes and other uterine cells to keep the placenta working properly.

The behavior of the maternal immune cells is surprising. The placenta, which derives half of its genes from the father, is inherently foreign to the mother. This foreignness raises the question of how the placenta escapes rejection by immunological processes that would otherwise recognize and destroy such an invader, as in the case of a conventional organ transplant. Investigators now know that changes in a mother's immune system help her "tolerate" the placenta. Local processes that operate within the uterus also play a part. For example, research on mice published in 2012 by one of us (Erlebacher) showed that the leukocytes that usually reject organ transplants are unable to accumulate in the uterine wall near the invading placenta.

The mother's body does not simply tolerate the placenta, however. It actively promotes the invasive growth of fetal tissues. Starting in the 1980s, for example, researchers discovered that a type of leukocyte called a natural killer cell is abundant on the uterine side of the maternal-fetal interface. As a general rule, these specialized cells kill tumors and virus-infected cells. But in the 1990s investigators led by B. Anne Croy, now at Queen's University in Ontario, made the counterintuitive discovery that natural killer cells also support placental development—in particular, the remodeling of uterine arteries by cytotrophoblasts. Presumably uterine natural killer cells produce substances that promote the loss of the original maternal cells

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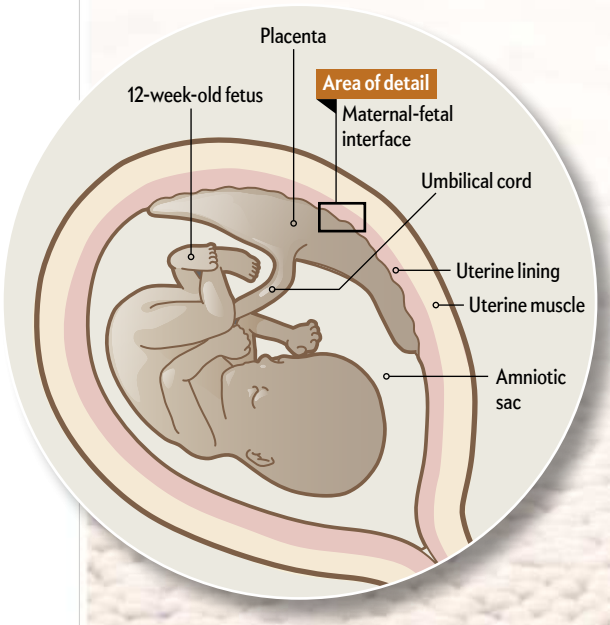
Pregnancy in Progress

A successful pregnancy depends on activities at the interface between a pregnant woman's body and her fetus, where the placenta (a product of embryonic cells) meets the uterine wall. Proper development and functioning of this interface, including delivery of oxygen, nutrients and fluid from the maternal blood to the fetus (an "embryo" becomes a "fetus" at the end of the eighth week after fertilization), require coordination among the cells of the placenta, the uterus and, new findings show, the mother's immune system. The flow of maternal blood to the placenta normally begins 10 to 12 weeks after fertilization.



Decidual cells composing uterine lining (*not all cells are shown to scale in this illustration*)

Spiral artery

Invasion of the Uterus

1 Artery Remodeling
The placenta contains branching structures called chorionic villi, which are composed of cells called trophoblasts. The surface of the villi consists of trophoblasts that have fused (forming what are termed syncytiotrophoblasts); these cells in turn sit on a layer of trophoblasts that do not fuse (known as cytotrophoblasts). Some of the cytotrophoblasts break through the fused-cell layer to invade the uterine spiral arteries, where they mimic the mother's own blood vessel cells.

2 Materials Exchange
The mother's transformed arteries open into the spaces between the chorionic villi branches (most of which are free-floating rather than anchored to the uterine lining by cytotrophoblasts), bathing the syncytiotrophoblasts in maternal blood and facilitating the exchange of materials between the mother and fetus. Uterine veins carry deoxygenated blood away from these spaces.

Oxygenated maternal blood

Cytotrophoblast

Syncytiotrophoblast

Transfer of nutrients and oxygen

Anchoring chorionic villus with invading cytotrophoblasts

Transfer of wastes, carbon dioxide and hormones

Floating chorionic villi

Fetal blood

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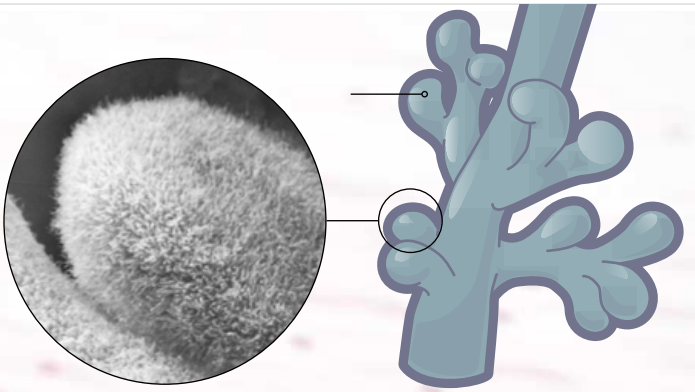
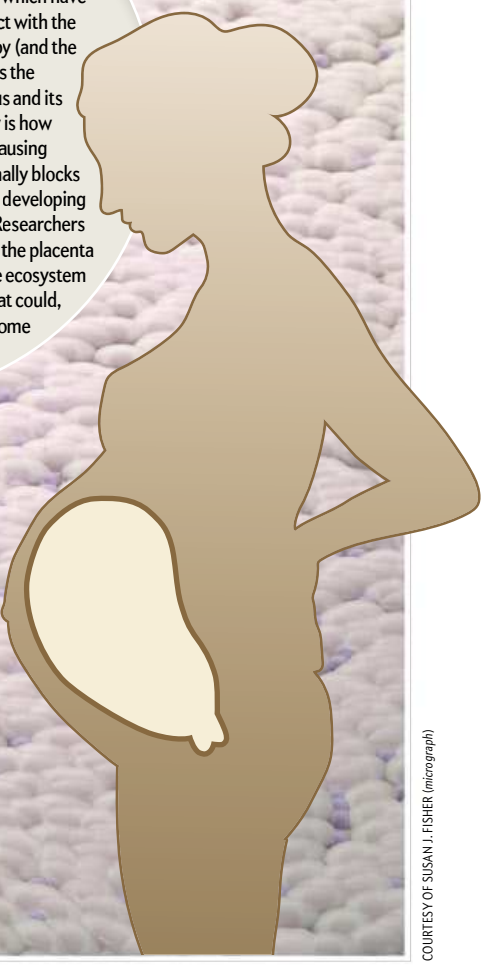
The Benefit of Branches

The size and complexity of the placenta's chorionic villi increase as the treelike organ grows and develops branches. As the branches form, they quickly become covered with micro branches only a tenth of a micron in length, resulting in an enormous overall increase in surface area. Only a slim layer of placental cells separates maternal blood delivered to the spaces between chorionic villi from fetal blood in vessels of the chorionic villi. This arrangement maximizes the exchange of oxygen, nutrients, hormones and waste products. Before blood flow to the placenta begins, the fetus receives nourishment from material secreted by the uterine lining.



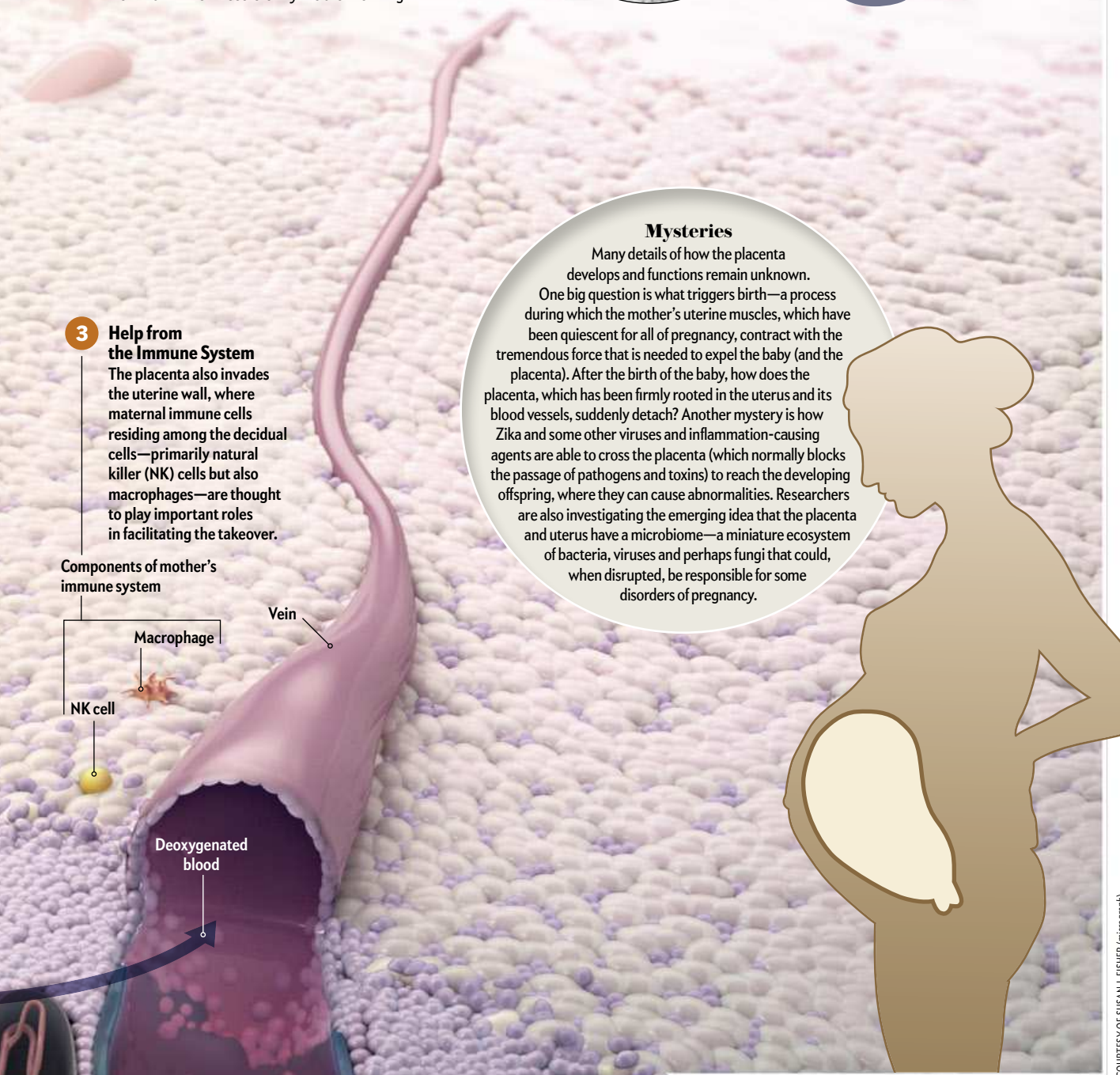
Mysteries

Many details of how the placenta develops and functions remain unknown. One big question is what triggers birth—a process during which the mother's uterine muscles, which have been quiescent for all of pregnancy, contract with the tremendous force that is needed to expel the baby (and the placenta). After the birth of the baby, how does the placenta, which has been firmly rooted in the uterus and its blood vessels, suddenly detach? Another mystery is how Zika and some other viruses and inflammation-causing agents are able to cross the placenta (which normally blocks the passage of pathogens and toxins) to reach the developing offspring, where they can cause abnormalities. Researchers are also investigating the emerging idea that the placenta and uterus have a microbiome—a miniature ecosystem of bacteria, viruses and perhaps fungi that could, when disrupted, be responsible for some disorders of pregnancy.



3 Help from the Immune System

The placenta also invades the uterine wall, where maternal immune cells residing among the decidual cells—primarily natural killer (NK) cells but also macrophages—are thought to play important roles in facilitating the takeover.



COURTESY OF SUSAN J. FISHER (*micrograph*)

Illustration by AXS Biomedical Studio

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that line the arteries, thus facilitating the subsequent takeover of these vessels by placental cells.

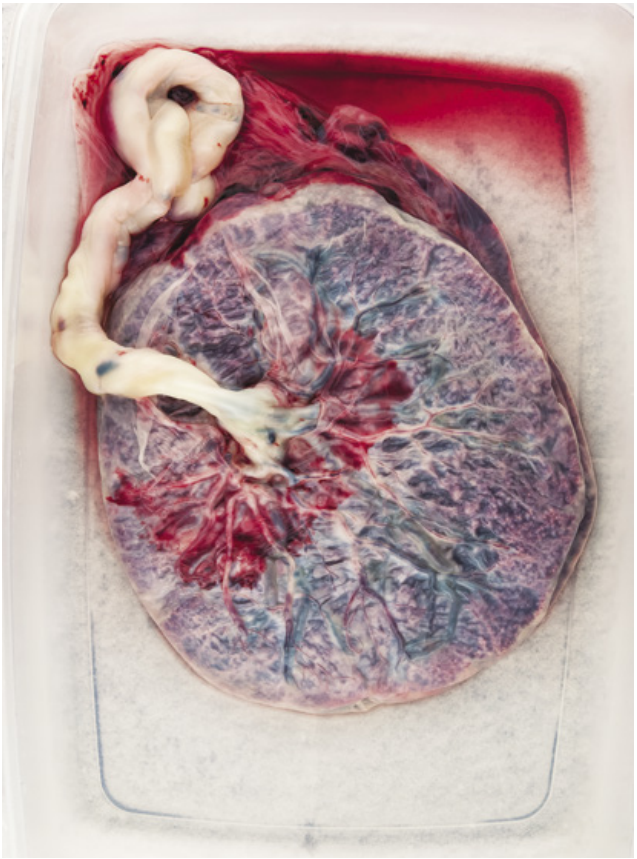
PROBLEMS AT THE INTERFACE

GIVEN THE BREAKNECK PACE of placental development and the many cell types that make up the placenta and the uterine wall, it should perhaps come as no surprise that errors can arise during the formation of the maternal-fetal interface. Such mistakes can cause a diverse array of pregnancy complications, the most important of which are termed the "great obstetrical syndromes." They include preterm birth (delivery occurs before 37 weeks of pregnancy), intrauterine growth restriction (the baby is smaller than expected), and preeclampsia (the mother suddenly develops high blood pressure and vascular damage).

Recent studies of the placenta have helped elucidate the origins of some of these conditions. Preeclampsia, for example, was once known as toxemia: physicians believed that it occurred because the placenta released toxins into the mother's blood. Although the precise mechanisms that cause preeclampsia—which affects about 8 percent of first-time pregnancies—are still unknown, investigators have found that it is associated with distinct structural deformities in the maternal-fetal interface. Experts now believe that the condition stems from an insufficient cytotrophoblast invasion of the uterine arteries during the first half of pregnancy. The inadequate blood supply restricts fetal growth. Eventually the abnormally developed placenta does release substances that are toxic to the mother, particularly to her circulatory system, but these toxins do not appear to be the root cause, as was previously thought. Rather they are likely a consequence of the disease. If left untreated, preeclampsia can lead to serious or even fatal damage to both mother and child.

Exactly why the placenta fails to work properly in cases of preeclampsia remains obscure. The dysfunction may arise within the cytotrophoblasts or the various maternal cells, or some combination thereof. Intriguingly, the ability of natural killer cells to detect foreign tissue may be a contributing factor. Research conducted by Ashley Moffett, a specialist in reproductive immunology at the University of Cambridge, suggests that if the placenta and mother are too similar immunologically, the natural killer cells may not be able to fully support the replacement of maternal cells from the inner lining of the uterine arteries with cells from the placenta.

Another of the great obstetrical syndromes—preterm birth—has recently raised alarm bells because its incidence is increasing worldwide. According to the Centers for Disease Control and Prevention, this disorder now affects about one in 10 pregnancies in the U.S. Although intrauterine infection can trigger early delivery, many preterm births have no clear-cut cause. In fact, scientists still do not understand what triggers a *normal* birth at the end of pregnancy, one of the major unsolved questions in human biology. Presumably a "clock" counts down the 280 days of human gestation. We know that when the alarm goes off, it initiates an inflammatory cascade within the uterus that is probably the immediate cause of uterine contraction and delivery. But where is the clock ticking? Is it in the fetus, placenta or uterus? It is easy to imagine that defective placental development early in gestation might gum up the inner workings of a birth clock, although this idea remains speculative.



NORM BARKER

THIS SIDE of the placenta, shown after birth with the umbilical cord, faced the baby during pregnancy. The flip side, which resembles a blood-filled sponge, was attached to the mother's uterine wall.

The great obstetrical syndromes overlap in their signs and in their underlying mechanisms. Shallow cytotrophoblast invasion, which is consistently associated with preeclampsia, for example, is also a feature of intrauterine growth restriction and some cases of preterm birth. A better understanding of how problems at the maternal-fetal interface diverge into very different complications might suggest ways to intervene more effectively.

LASTING IMPRINTS

SUCH MAJOR GESTATIONAL IRREGULARITIES have obvious harmful effects on newborns, from treatable conditions that require hospitalization in neonatal intensive care units to permanent neurological impairments. The ill effects of an inadequate environment for fetal growth do not end with infancy, however; they may manifest decades later as adult diseases, and there is reason to believe that flaws in placental function play a part here, too.

The idea that conditions in the womb can affect health in later life is termed the fetal origins hypothesis. It was first proposed in the 1980s by the late British epidemiologist David Barker to try to explain the high incidence of cardiovascular disease and diabetes in poor areas of England. Barker noted that adults with these chronic conditions were more likely to have been underweight at birth, possibly reflecting suboptimal nutritional status. Some investigators think that malnutrition and faulty placental function may change the way a baby's genes direct its development during pregnancy—but the mechanics that underlie this process are unknown. Epidemiological

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A successful pregnancy relies on the interchange between the maternal cells in the uterine tissue and the invading branches of the placenta.

evidence also strongly indicates that children born to women who contract certain infections—such as an influenza virus—during pregnancy have an increased risk of neurodevelopmental and psychiatric disorders, including autism, bipolar disorder and schizophrenia.

A mouse study published in 2016 by immunologists Dan R. Littman of New York University and Jun R. Huh, now at Harvard Medical School, suggests how a flu infection might subtly change the course of brain development in a way that only becomes evident years or decades later. Previously scientists knew that virus-mimicking agents that cause systemic inflammation in pregnant mice also cause autismlike behaviors in their offspring. Littman, Huh and their colleagues showed that the inflammation-inducing agent is interleukin-17 (IL-17) and that it is produced by the mother's immune cells. Using sophisticated imaging techniques, the team showed that the protein was directly responsible for subtle structural changes in the brains of affected mice.

But how does maternal IL-17 cross the placenta to reach the fetal brain when many other molecules of a similar size cannot get through? One possibility is that, for some reason, the placenta actively transports IL-17 from maternal blood to the fetal circulatory system, enabling it to access the brain. Another intriguing possibility is that some of the mother's cells that are making IL-17 themselves traverse the placenta to reach the fetus.

CROSSING OVER

THE ZIKA PANDEMIC is a graphic illustration of the damage that can be done when a virus that infects the mother learns how to cross the placenta. At the moment, though, researchers have more questions than answers as to how Zika causes the health problems that have arisen in affected babies.

Given that investigators only recently made the association between Zika virus infections during pregnancy and adverse outcomes, it is not surprising that very little is known about how Zika reaches the fetus. Even the rate of birth defects is unclear and seems to vary by location. In a U.S.-based study published in January 2017 in *JAMA,* researchers at public health departments and the CDC found birth defects in only 6 percent of the fetuses or infants of mothers with possible Zika infections. A Brazilian study published the previous month in the *New England Journal of Medicine,* however, suggested that almost half of infected fetuses could have some form of damage. In addition, some Brazilian babies have developed neurological problems after initially being evaluated as normal. Because Zika's most damaging effects—particularly microcephaly—seem to be more prevalent in Brazil than elsewhere, some researchers have speculated that a chemical in the Brazilian environment may weaken the placenta and make it more susceptible to Zika. Alternatively, simultaneous infection with another microbe prevalent in Brazil might be the culprit.

Also in question is how Zika reaches the fetus. Does it plow through the placenta from the maternal side, infecting every cell type in its way, or is it chaperoned by particular cell types—such as maternal immune cells? Alternatively, we know that certain pathogens can ascend from the vagina to the uterus, thereby gaining access to fetal tissues. However the Zika virus reaches the fetal tissues, it establishes a firm foothold once there: molecular pathologists at the CDC have reported that the Zika virus can persist in the placenta for months and can continue to replicate in an infant's brain even after birth.

Zika is not, of course, the only pathogen that can cross the placenta and harm the fetus. Around the globe, an estimated 100,000 babies are born every year with congenital rubella, which can cause deafness, eye abnormalities, heart disease and other serious problems. Malaria, herpes and Ebola can all cause lethal damage during pregnancy. The precise means by which they invade the fetus remain to be determined. But it appears likely that some pathogens are better able to infect the placenta's trophoblasts, particularly in early gestation. Immune defense mechanisms at the maternal-fetal interface are probably also poor gatekeepers at times, given that the uterine lining has two inherently contradictory jobs. On the one hand, it must protect the fetus and placenta from infection. On the other hand, as alluded to earlier, it must prevent maternal immune responses from becoming so robust that the placenta is harmed.

With so much left to learn about the placenta and pregnancy, the Eunice Kennedy Shriver National Institute of Child Health and Human Development launched in 2014 the Human Placenta Project, which aims to understand this enigmatic organ that "influences not just the health of a woman and her fetus during pregnancy, but also the lifelong health of both." Along with efforts to cure HIV, cancer and cardiovascular disease, understanding the placenta should be given the highest priority on the national health research agenda. SA

Adrian Erlebacher is a professor in the department of laboratory medicine at the University of California, San Francisco, School of Medicine. He conducts studies in mice to tease out the properties of the pregnant uterus that enable it to immunologically tolerate the placenta.

Susan J. Fisher is a professor in the department of obstetrics, gynecology and reproductive sciences at the U.C.S.F. School of Medicine. Her laboratory explores placenta formation in normal human pregnancy and how flaws in the process contribute to complications.

MORE TO EXPLORE

The "Great Obstetrical Syndromes" Are Associated with Disorders of Deep Placentation. Ivo Brosens et al. in *American Journal of Obstetrics and Gynecology,* Vol. 204, No. 3, pages 193–201; March 2011.

Immunology of the Maternal-Fetal Interface. Adrian Erlebacher in *Annual Review of Immunology,* Vol. 31, pages 387–411; 2013.

Uterine NK Cells: Active Regulators at the Maternal-Fetal Interface. Ashley Moffett and Francesco Colucci in *Journal of Clinical Investigation,* Vol. 124, No. 5, pages 1872–1879; May 1, 2014.

Placenta: The Forgotten Organ. Emin Maltepe and Susan J. Fisher in *Annual Review of Cell and Developmental Biology,* Vol. 31, pages 523–552; 2015.

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Men and women have different ways of speaking, but research reveals the conversational gender divide is not as stark as it seems

By Deborah Tannen

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WHY DON'T MEN LIKE TO STOP AND ASK DIRECTIONS? This question, which I first addressed in my 1990 book *You Just Don't Understand: Women and Men in Conversation,* garnered perhaps the most attention of any issue or insight in that book. It appeared on cocktail napkins ("Real men don't ask directions") and became a staple of stand-up comics as well as jokes that made the rounds: "Why did Moses wander in the desert for 40 years?" and "Why does it take so many sperm to find just one egg?"

The attention surprised me. I had not known how widespread this experience was, but I included the asking-directions scenario because it crystallized key aspects of a phenomenon that, I had discovered, accounts for many of the frustrations that women and men experience in conversation. I have spent more than three decades collecting and analyzing thousands of examples of how women and men interact and have found that men's talk—both voice-to-voice and through social media—tends to focus on relative hierarchy, and women's tends to focus on relative connection. In other words, a man and woman might walk away from the same conversation asking different questions: he might wonder, "Did that conversation put me in a one-up or one-down position?" whereas she might wonder, "Did it bring us closer together or push us farther apart?"

But wait! All conversations, and all relationships, reflect a combination of hierarchy and connection—the two are not mutually exclusive but inextricably intertwined. All of us aspire to be powerful, and we all want to connect with others. Since the publication of *You Just Don't Understand,* I have continued to investigate the nuances of women's and men's ways of speaking to clarify how their conversational styles are different ways of reaching the same goals. In later work, I explored the context in which *women's* focus on hierarchy and *men's* on connection is most obvious and most intense: the family. In particular, sisters provide insight into relationships among women that are deeply influenced by competition as well as by connection.

So what does any of this have to do with asking for directions? The route to the answer may not yet be obvious, but read on, and I promise to get you there.

"MINE'S HIGHER" VS. "WE'RE THE SAME"

MY INTEREST in the linguistic differences between women and men grew from research I conducted early in my career on conversations between speakers of different ethnic and regional backgrounds. These interactions often led to misunderstandings because members of different groups had contrasting assumptions about what should be said and the appropriate way to say it. I sensed, and later showed, a parallel pattern in conversations between women and men—a gender-based culture clash.

I often illustrate this phenomenon using video clips of preschoolers at a day care center. In one scene, four little boys are sitting together, talking about how high they can hit a ball. "Mine's up to there," one small boy declares, raising his arm above his head. "Mine's up to the sky," a second responds, pointing higher. A third boy counters, "Mine's up to heaven!" Then the fourth boy offers: "Mine's all the way up to God." These boys' verbal exchange is obviously a game of hierarchy, as each one's claim tops the preceding one.

I contrast this video clip with another from the same preschool: two little girls are sitting at a small table, drawing. One girl suddenly raises her head, looks at the other, and says (apparently referring to

IN BRIEF

Men's talk tends to focus on hierarchy—competition for relative power. Women's tends to focus on connection—relative closeness or distance.
But all conversations, and all relationships, reflect a combination of hierarchy and connection. The two are not mutually exclusive but inextricably intertwined. All of us aspire to be powerful, and we all want to connect with others. Women's and men's conversational styles are simply different ways of reaching the same goals.
The context in which women's focus on hierarchy and men's on connection is most obvious and most intense: the family. In particular, sisters provide insight into relationships among women that are deeply influenced by competition and hierarchy as well as connection.

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contact lenses), "Did you know that my babysitter, called Amber, has already contacts?" The second girl looks puzzled at first but quickly gathers herself together and announces, with apparent relish, "My mom has already contacts, and my dad does, too!" The first girl laughs with glee at this echo response, which even mirrors the first girl's odd syntax ("has already" rather than "already has"). After a pause, during which both girls return to drawing, the first one exclaims with delight, "The *same?!*" Being the same is as pleasing to her as topping one another is to the boys.

Although the specific conversational moves—topping versus matching—are different, what these contrasting conversations have in common is that they are rituals: self-evident assumptions about how the conversations should go and what a reasonable remark or response should look like. As with cross-cultural communication, we do not recognize them as rituals until we talk to others who do not share our assumptions.

Parents tell me that recognizing these as gender-related patterns in their children helps them deal with otherwise baffling behavior. For example, a woman recalled overhearing three little boys—her son and two of his friends—talking in the backseat as she was driving. One boy said, "When we went to Disneyland, we stayed three days." The second boy said, "When we went to Disneyland, we stayed four days." Then her son said, "We're going to move to Disneyland!" She was troubled to hear him utter an obvious untruth. Should she instruct her son not to tell lies? I assured her that the boys knew that her family was not going to move to Disneyland. But her son won that round.

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GIRLS AND WOMEN like to match. When they talk, they emphasize their similarities to build intimacy.

A father told me about a similar confusion upon overhearing a conversation between his little girl and her friend. The friend had said, "I have a brother named Benjamin and a brother named Jonathan." His daughter responded, "I have a brother named Benjamin and a brother named Jonathan, too." But she didn't. Her father wondered why she would say such a thing. I explained that she was simply offering a matching experience as a sign of goodwill, to reinforce the friendship.

The contrasting focus on connection versus hierarchy also sheds light on innumerable adult conversations—and frustrations. Say a woman tells another about a personal problem and hears in response, "I know how you feel" or "The same thing happens to me." The resulting "troubles talk" reinforces the connection between them. (Indeed, some women feel they have to dig up problems to tell friends to maintain intimacy.) Because this is not a conversational ritual he is used to, a man may well misread her conversational gambit as a request for help solving the problem. The result is mutual frustration: she blames him for telling her what to do and failing to provide the expected comfort, whereas he thinks he did exactly what she requested and cannot fathom why she would keep talking about a problem if she does not want to do anything about it.

Similar scenarios play out at work, where mutual misinterpretations may have career-altering consequences. For example, if a woman's boss overhears her telling a subordinate, "Could you do me a favor and get me a copy of that report?" he may think she lacks confidence. It appears to him as if she does not feel she has a right to ask her subordinate to do something. But the truth is probably the exact opposite. She knows the subordinate has to do what she asks. Her locution "do me a favor" is simply a way of not flaunt-

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ing the power she obviously has—and thus saving face for the subordinate. If men often mishear women's ritual indirectness as lacking confidence (or even competence), women often misinterpret *less* indirect rituals as overbearing—and also lacking in confidence. Her thinking goes: he must really lack confidence if he has to throw his weight around like that.

Which takes us back to the woman and man who have different assumptions about asking directions. At the time that I first used this example, before GPS and smartphone technology made it possible to easily access route information on the go, the debate over whether to ask directions regularly took place in cars and often still does. From the woman's point of view, asking directions means making a fleeting connection to a stranger and getting where you are going without losing anything. From the man's perspective, he would be putting himself in a one-down position to a stranger—an uncomfortable experience. He might even believe the effort is counterproductive because a stranger who does not know the way will be similarly motivated by a reluctance to appear one-down and send them on a wild-goose chase. For both reasons, it makes sense to avoid this discomfort and spend 10 minutes—or 20 or 30—finding the way on his own.

OLDER SISTERS often act dominant to younger sisters, speaking to them in ways more often expected of boys and men.

DIFFERENT STYLES, SIMILAR GOALS

DESPITE THESE DIFFERENCES, women's and men's conversational styles are more alike than they may appear. Although these styles may seem opposite, they can be used for similar purposes. Boys and men are also concerned with connection and girls and women with power, even as they may have different ways of pursuing these goals.

Verbal rituals that focus on connection often involve affirming sameness, as we saw in the little girls' exchange about contact lenses and in the familiar responses: "The same thing happened to me" and "I'm the same way." Yet the contrasting ritual, "That's nothing! Here's what happened to me…," which is typically associated with men—and interpreted as competitive—can also create connection by implying, "You shouldn't feel bad about what happened to you, because what happened to me was worse." In other words, "topping" each other can be another way to commiserate.

Similarly, for girls and women, what appears on the surface to be aimed at connection can also be a way to exert power. Linguist Amy Sheldon of the University of Minnesota has investigated this process by videotaping preschool children playing in same-sex groups of three. She found that both boys and girls pursued their own goals, but whereas the boys she taped were obvious about thwarting another's goals, the girls often did so in ways that appeared to honor the other girls' goals as well. In one example, two girls, Eva and Kelly, were not eager to include the third girl, Tulla, in their play. Instead of telling Tulla outright that she could not play, they included her but assigned her a role that precluded her participation: "You can be the baby brother, but you aren't born yet." Sheldon emphasizes that this is a highly assertive move, even as it maintains the appearance of accommodating Tulla's wish to be part of the game.

In this instance, the children's behavior is not a clear on-or-off application of hierarchy or connection but a blending of both. We could say that Eva and Kelly exercised power to keep Tulla from participating but also honored the connection by assigning her a role.

In contrast, Sheldon observed that when boys played, they tended to insist more overtly on their own goals and even to threaten physical force. For example, when one boy, Nick, wanted to cut a plastic pickle that another boy had, he screamed, "I *have* to cut! I want to cut it! It's mine!" Sheldon stresses, however, that although boys and girls tended to use more of one strategy or another, the difference was not absolute but of degree. Boys did sometimes attempt to compromise, and girls did at times attempt physical force to get their way.

Sheldon's research reminds us that patterns, no matter how real, are never absolute. Again, the asking-directions example is instructive. I didn't realize how common that scenario is because my husband does stop and ask directions, whereas I am the one who says, "I'd rather find it myself on the map." In this respect, he and I are not typical, as many of us are not typical of our genders, cultures, regions or any other group to which we belong.

Gender differences are a matter of relative *focus* on connection and hierarchy, as we all want to accomplish both goals to some extent. We are always engaged in negotiations over connection and relative power. Eva and Kelly served both goals when they included Tulla—and kept her from participating. Similarly, the boys who verbally competed about how high they could hit a ball also created connection by agreeing on the type of verbal game to play. To understand gender patterns, then, rather than asking, "Does this way of speaking serve hierarchy or connec-

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tion?" we need to ask, "How does this way of talking reflect the interplay of connection and hierarchy?" And nowhere can this interplay be better explored than in the context that is both universal and fundamental: the family.

FAMILY TIES

FAMILY COMES WITH built-in hierarchy as well as built-in connection. The hierarchy between parents and children is self-evident, but the same is true of siblings. Even though we use the phrases "like sisters" and "like brothers" to describe friendships that are close and equal, actual sibling relationships are defined not only by the connection of shared family but also by the hierarchy of birth order. I have been particularly intrigued by sisters—not only because I have two but, most important, because in sisters we see a relationship between women that is deeply competitive and hierarchical.

In *Having Our Say,* the Delany sisters' 1993 best-selling memoir, Bessie Delany is quoted as saying, "Sadie doesn't approve of me sometimes. She looks at me in that big-sister sort of way." When she said this, Bessie was 101, and Sadie was 103. Elsewhere in the book, Sadie says, "If she lives to 130, I'll just have to live to 132, so I can take care of her." Their relationship was still shaped by the two years separating them, despite the century they had lived.

These centenarians' comments reflect dynamics I heard from many of the more than 100 women I interviewed about their sisters for my book *You Were Always Mom's Favorite! Sisters in Conversation throughout Their Lives,* as well as comments I have heard about brothers: older siblings were often seen as protective but also judgmental. After all, these qualities are two sides of the same coin. "Judgmental" means you see how others can improve themselves and their lives—and tell them. We all often think of ways our friends, relatives and even strangers could do things better. But we usually don't tell them what we think—unless we feel responsible for them. Parents often come across as judgmental to children because they feel it is their right, if not their obligation, to make sure their children's lives go as well as possible, which means letting them know the ways they can improve. Such offers of advice, however, no matter how well-meaning (in other words, focused on connection), are often heard as criticism—and therefore as put-downs. The giver of advice is one-up, superior in knowledge and, by virtue of exercising the right to tell the other what to do, also superior in rank.

Similarly, many older sisters speak to younger siblings with commanding and unambiguous authority—ways of speaking that are more often associated with boys and men. One woman told me when she was small, she and her older sister played a game they called "mop." She was the mop. Her sister would grab her by the feet and drag her around the house, her long hair sweeping the floor like a mop. Several other women recalled their older sisters organizing and directing plays. A typical casting setup was: "I'll be the princess; you be the frog." In my own family, my father overheard me asking my sister, when I was about four and she about six, "Mimi, can I play in your backyard?" Clearly, I did not question the authority that my older sister had assumed in her dealings with me.

At the same time, closeness is the holy grail of sister relationships, as it tends to be for girls and women in other contexts as well. When speaking to women about their sisters, I often heard "I wish we were closer" but never "I wish we weren't so close." Their comments also generally reflected the assumption so common among women that troubles talk is critical for intimacy. Women told me they were deeply hurt to learn that a sister had kept important personal information secret. Whereas a brother (or a father) might say, "He told us when he was ready," sisters (like mothers) often feel, "I thought we were closer than that" or "If she'd told me, I could've helped."

A powerful rivalry often accompanies sisterly ties—but it can take the form of competition for connection. Sisters often feel acutely competitive about who knows what about family members' secrets—or who knows first. Correspondent Juju Chang, in a segment of the news program *20/20* that was based on my book, explained that she and her three sisters have learned that if one of them has important personal information to impart—news of an engagement or a pregnancy, for example—they must set up a conference call so all three sisters will learn the news at the same time. Otherwise, the sister who is called first will seem to be favored, and the others will feel slighted.

Thus, sisters are often very competitive, and hierarchy is built into their relationship by virtue of birth order. And brothers are often very close and have connection built into their relationship by virtue of shared family. Sisters and brothers tend to vie, however, for dominance in different arenas. Whereas sisters may compete about who knows more personal information about family members, brothers may compete about who knows more facts about impersonal information such as computers or history.

Family relationships make clear that closeness is not opposite or even distinguishable from hierarchy and competition. Indeed, one reason that older sisters feel so comfortable bossing younger ones around and giving them advice is precisely because there is a strong connection between them. In addition, the deep love between older and younger siblings, like that between parents and children, results in part from the acts of caretaking and the experience of being taken care of that these roles entail.

Listening in on conversations among family members reveals a unique blend of authority and intimacy in talk among women as well as among men. It highlights the ways in which gendered conversational patterns can be different routes to the same goal: finding the right balance of closeness and distance while simultaneously negotiating relative power. SA

Deborah Tannen is a University Professor and a professor of linguistics at Georgetown University and author of many books, including *You're the Only One I Can Tell: Inside the Language of Women's Friendships* (Ballantine Books, 2017).

MORE TO EXPLORE

Talking from 9 to 5: Women and Men at Work. Deborah Tannen. William Morrow Paperbacks, 2001.
I Only Say This Because I Love You: Talking to Your Parents, Partner, Sibs and Kids When You're All Adults. Deborah Tannen. Ballantine Books, 2002.
You're Wearing THAT? Understanding Mothers and Daughters in Conversation. Deborah Tannen. Ballantine Books, 2006.
You Just Don't Understand: Women and Men in Conversation. Deborah Tannen. William Morrow Paperbacks, 2007.
That's Not What I Meant! How Conversational Style Makes or Breaks Relationships. Deborah Tannen. Harper Perennial, 2011.

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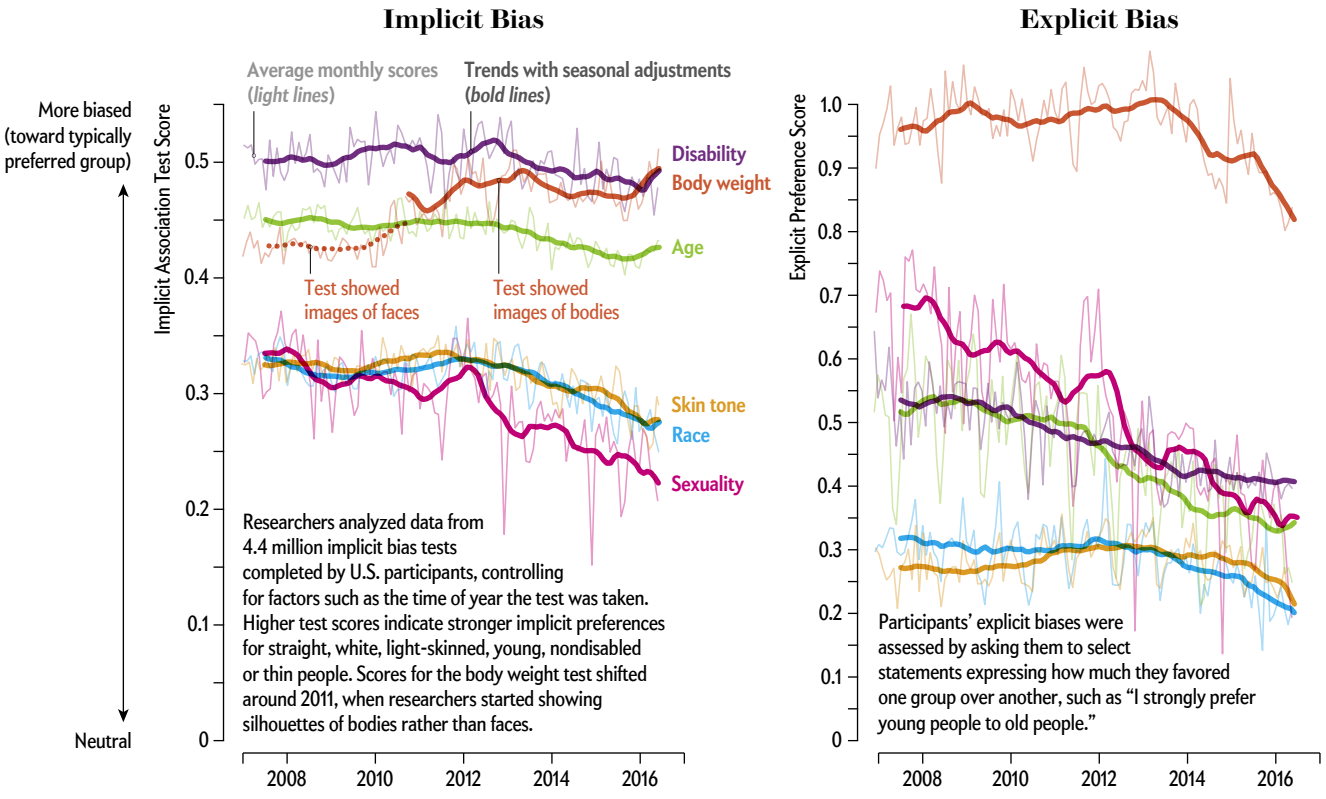
Implicit Bias
Explicit Bias
More biased (toward typically preferred group)
Neutral
Implicit Association Test Score
Average monthly scores (light lines)
Trends with seasonal adjustments (bold lines)
Disability
Body weight
Age
Test showed images of faces
Test showed images of bodies
Skin tone
Race
Sexuality
Researchers analyzed data from 4.4 million implicit bias tests completed by U.S. participants, controlling for factors such as the time of year the test was taken. Higher test scores indicate stronger implicit preferences for straight, white, light-skinned, young, nondisabled or thin people. Scores for the body weight test shifted around 2011, when researchers started showing silhouettes of bodies rather than faces.
Explicit Preference Score
Participants' explicit biases were assessed by asking them to select statements expressing how much they favored one group over another, such as "I strongly prefer young people to old people."
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
2008
2010
2012
2014
2016

BIASES AREN'T FOREVER

Implicit prejudice against certain groups is declining

By Matthew Hutson

Psychologists have lots of evidence that implicit social biases—our automatic, knee-jerk attitudes associated with specific races, sexes and other categories—are widespread, and many assumed they do not evolve. The feelings are just too deep. But a recent study finds that over roughly the past decade, both implicit and explicit, or conscious, attitudes toward several social groups have grown warmer.

The study used data from a standard test of implicit attitudes collected via a Web site called Project Implicit. Participants were asked to quickly press a certain computer key in response to positive words, such as "happy," and a different key in response to negative words, such as "tragic," that appeared on a screen. These words were interspersed with images or words that represented two categories of people, such as blacks and whites, and participants were asked to flag these using the same keys. Faster reactions when, for example, black rather than white faces shared a key with negative words suggested a racial bias.

Tessa Charlesworth and Mahzarin Banaji, psychologists at Harvard University, analyzed more than four million results collected over a 10-year period from U.S. adults who had taken implicit association tests for sexuality, race, skin tone (in which faces differ in color but not shape), age, disability and body weight. Respondents also answered questions on the screen asking them to explicitly rate how much they liked people in each of the categories.

In line with previous findings, explicit bias decreased in all six categories from 2007 through 2016; the drop ranged from 49 percent (for sexuality) to 15 percent (for body weight). But more surprisingly, implicit bias also decreased—by 33 percent for sexuality, 17 percent for race and 15 percent for skin tone (*graphic*). Most of the reductions occurred in all generations, the researchers reported in a study published online in early 2019 in *Psychological Science*. "It's a really cool paper," says Keith Payne, a psychologist at the University of North Carolina at Chapel Hill, who has found similar bias reductions in his own work. "I think it's going to start a lot of conversations."

Charlesworth and Banaji also found, however, that implicit biases about age and disability did not change over time, and those against overweight people nudged up by 5 percent.

Several factors might explain the discrepancies among categories, the researchers say. In their data set, implicit biases for race, skin tone and sexuality were lower to begin with than those for age, disability and body weight. And the types of implicit biases that decreased the most are also the biases that have received more societal attention. Meanwhile the stigma associated with obesity may have increased in recent years.

Next, the team plans to explore implicit and explicit attitude change across demographics and geographical regions, as well as whether there is evidence that trends have changed since the 2016 U.S. presidential election.

SOURCE: "PATTERNS OF IMPLICIT AND EXPLICIT ATTITUDES, VOL. I: LONG-TERM CHANGE AND STABILITY FROM 2007 TO 2016," BY TESSA E. S. CHARLESWORTH AND MAHZARIN R. BANAJI, IN *PSYCHOLOGICAL SCIENCE*, VOL. 30, NO. 2; FEBRUARY 2019

Graphic by Amanda Montañez

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TIME FOR WOMEN LEADERS

The gender gap in leadership narrows when groups spend more time together

By Matthew Hutson

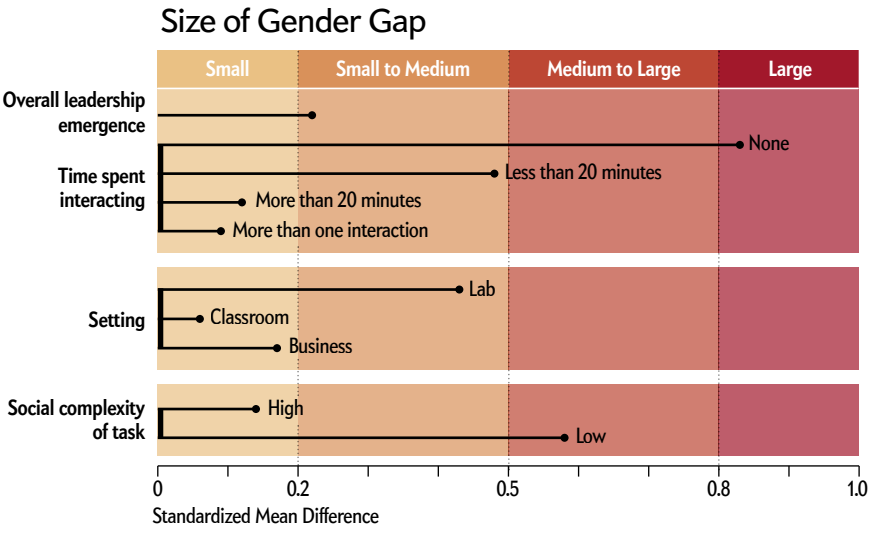
Only 28 percent of American CEOs are women. To find out why such a gap exists, a study published in 2018 in *Personnel Psychology* analyzed more than 100 papers on leadership emergence published between 1957 and 2017. In the papers, samples of students or co-workers were asked to select group leaders or to rate one another on the extent to which they led a group. Some of the papers also measured group participation and personality traits such as assertiveness. As predicted, men emerged as leaders more often than women. But that gap varied depending on the length of interaction and other factors (*graphic*).

The data suggest that men were more likely overall to be chosen or rated as leaders, in part because they had more assertive personalities and thus spoke up more. Men and women were equally likely to emerge as leaders, however, when groups interacted for more than 20 minutes—possibly, the researchers write, because members relied less on gender stereotypes as they became better acquainted.

Other research shows that male and female leaders perform equally well. Considering the gender gap at the top of organizational charts, "that's a ton of human capital that organizations are ignoring," says Katie Badura, a management researcher at the Georgia Institute of Technology and the lead author of the study. She says women should not be asked to change their behavior as a way of addressing this situation; rather, organizations should train employees to change their perspectives.

Alice Eagly, a psychologist at Northwestern University, who conducted a similar analysis three decades ago, praised the project's large scale. Eagly advocates for women's empowerment, but she also has advice for men: "Be less dominant. Let other people have some time to talk."

Matthew Hutson is a freelance science writer based in New York City and author of *The 7 Laws of Magical Thinking*.



People are generally less likely to recognize leadership qualities in women than in men. But this gender gap shrinks when a group interacts for longer periods of time, a study shows. Researchers also looked at other variables, including the setting and social complexity of tasks being studied. Laboratory settings had a larger gender gap than business ones, but once the length of time employees interact with one another was considered, the gap became wider in business settings. This indicates that whereas length of interaction time is important, business environments may have additional factors that perpetuate the gender gap. Groups engaged in socially complex activities—such as innovative problem-solving—exhibit a relatively small gender gap, but this disappeared after accounting for other factors.

Men and women were equally likely to emerge as leaders when groups interacted for more than 20 minutes because members relied less on gender stereotypes as they became acquainted.

SOURCE: "GENDER AND LEADERSHIP EMERGENCE: A META-ANALYSIS AND EXPLANATORY MODEL," BY KATIE L. BADURA ET AL., IN *PERSONNEL PSYCHOLOGY*, VOL. 71, NO. 3; AUTUMN 2018

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HOW CAPTIVES CHANGED THE WORLD

Stolen people—mostly women and children—were a driving force in the evolution of modern society

By Catherine M. Cameron

Illustration by Katie Edwards

IN BRIEF

Although small-scale societies are often depicted as communities of people who saw one another as equals, most of them actually contained a number of marginalized individuals, many of whom were captives from other groups. **World history has long** ignored the lives of these stolen people. But analyses of early travelers' accounts and other reports indicate that they profoundly influenced their captors' societies. **Captives created** power and wealth—factors that helped lay the groundwork for a major social transition: the evolution of complex, state-level societies.

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AS THE ARMIES OF ISIS swept across Syria and northern Iraq in the summer of 2014, they overran villages of Yazidi people, whom they considered infidels. The soldiers killed Yazidi men and seized the girls and women. Girls as young as 12 became "wives"—sex slaves passed around among the ISIS fighters. The horror was all too familiar: the nightmare the Yazidi women have endured is that of captive women through the ages.

For the past decade I have studied captive taking in historical and ancient cultures. I am an archaeologist interested in social and demographic processes in small-scale societies of the type that scholars call "tribes" or "chiefdoms"—groups of fewer than 20,000 people who are related through blood or marriage and whose leaders have relatively limited power. Captives were ubiquitous in these societies: early travelers' accounts, ethnohistorical documents, ethnographies, captive narratives and archaeological reports describe captives in every corner of the world, from northern Europe to southern South America. My analyses of these early writings represent the first attempt at a cross-cultural examination of abduction and its consequences.

The worlds described in these documents contrast sharply with the idealized image of small communities of people who treated one another as equals. Instead most small-scale societies contained a number of individuals who did not have access to the same resources and benefits as other members of the group. Some of these disadvantaged people were orphans, incompetents or criminals, but most were captives from other groups. Indeed, in some small-scale societies stolen people might constitute up to 25 percent of the population. Because they had no kin in the groups they unwillingly joined, captives were automatically marginal; unless they were adopted or married into the group, native group members often did not even see them as human.

Although captives formed the lowest social stratum of the groups they entered, they nonetheless influenced these societies in profound ways. They introduced their captors to new ideas and beliefs from their natal group, fostering the spread of technologies and ideologies. And they played key roles in the creation of status, inequality and wealth in the groups that abducted them. These factors may well have laid the groundwork for the emergence of a much more sophisticated social structure: the state-level society, in which one person or a small group of people hold significant power and authority over a population numbering more than 20,000 and in which group membership is built not on kinship ties but on social class or residence within the boundaries of a nation-state. For all the misery they endured, captives changed the world.

TAKEN BY FORCE

PEOPLE TYPICALLY BECAME CAPTIVES through warfare or raids. During his first voyage to the Americas in 1492, Christopher Columbus heard about the fierce Kalinago people of the Caribbean's Lesser Antilles islands. Documents from the 15th and 16th centuries reveal that the Kalinago traveled hundreds of miles in their war canoes to attack other islands and steal their goods and people. The raiders ritually killed the adult males they took soon after returning home. Young boys were emasculated and used as slaves until they reached adulthood, at which point they were sacrificed. The young women entered Kalinago society as their captor's concubine or his wife's servant. The hunter-gatherers of the Northwest Coast of North America raided for captives to put to work as slaves or to trade for other goods. Nineteenth-century accounts describe fleets of war canoes carrying warriors who attacked neighboring groups or made longer-distance raids. They took mostly women and children but also men not killed in battle. From the eighth to the 11th centuries Vikings raided throughout the North Atlantic and the Mediterranean, taking large numbers of captives to enslave or sell. During the 12th to 16th centuries coastal chiefdoms in the Philippines sent slave-raider fleets across the region, attacking smaller groups. According to archaeologist Laura Junker of the University of Illinois at Chicago, the raiders returned with captive women whom they enslaved or married. The women worked in agricultural fields or made pottery or textiles for their master to trade.

A society's captives rarely attained equal status with the native-born. When warriors returned, those captives destined to be slaves almost always underwent a process that sociologist Orlando Patterson of Harvard University calls "social death," in which they were stripped of their natal identity and "reborn" as slaves. During this process slaves were often forced to adopt some visible mark of their servitude and received a new "slave name." The Conibo people of eastern Peru, for instance, cut the hair of female captives to give them short bangs that denoted slave status. They also replaced the captives' traditional clothing, which the Conibo considered immodest and savage. The Kalinago beat and insulted their new captives, cut their hair as a sign of servitude, and renamed them "female slave" or "male slave." Because they were ultimately sacrificed and consumed, the young male slaves were also called "my barbecue."

Early 19th-century accounts describe the traumatic destruction of the social and cultural identity of captives in Southeast Asia, including a Dutch sea captain taken by Iranun slavers from the Philippines. The slavers stripped him of his clothes and bound him hand and foot to the bottom of a boat. According to ethnohistorian James Warren of Murdoch University in Australia, such pirates beat their captives on the elbows and knees so they could not run or swim away. Tied up for months at a time, poorly fed and constantly abused, the captives eventually gave up hope of escape.

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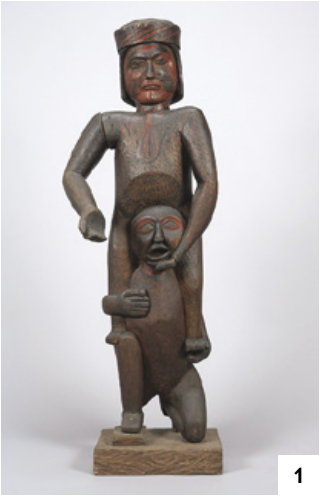
CAPTIVES in small-scale societies were typically put to work as slaves, as seen in a Northwest Coast Indian carving (*1*). Some, such as Helena Valero, who was abducted by the Yanomamö of the Amazon in the 1930s (*2*), became wives. The influence of captives on the groups they entered is visible in artifacts such as an Iroquois mask for a medicinal tradition that Huron captives may have introduced (*3*).



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In Northwest Coast societies, captives not only became slaves with no possibility of ever becoming members of their captor's society, but their children shared their fate. Like African slaves in the American South or industrial slaves in ancient Rome, slaves in Northwest Coast groups passed their status down to their offspring.

AGENTS OF CHANGE

ONE MIGHT EXPECT abused captives dragged into a new society to have little opportunity to transmit knowledge or skills to their captor's group. My cross-cultural study paints an emphatically different picture, however. People today tend to view small-scale societies as timeless and unchanging, but in truth, they were often eager to learn new things. Captives brought opportunities for social, economic and ideological progress, and their captors took full advantage of them.

A number of accounts hint that at least some captives were targeted for their technological know-how. English ship's armorer John Jewitt, taken in the early 19th century by the Mowachaht people, a Northwest Coast group, was spared in a lethal attack because the chief wanted the metal weapons Jewitt knew how to make. Jewitt, who detailed his ordeal in a memoir published in 1815, also showed his captors how to wash soiled clothes rather than discard them, although Jewitt himself had to do the washing. Helena Valero, who was kidnapped by the Yanomamö of the Amazon in the 1930s, when she was a child, reported that her abductors were furious when she told them she did not know how to make metal tools. She recounted her years with the tribe in a 1965 book, noting, "The women said 'She is a white woman, she must know; yet she doesn't want to make clothes, machetes, or cooking pots for us; hit her!'" But the headman and one of Helena's co-wives defended her, and she survived. Metalworking skills were similarly prized among the Germanic tribes of northern Europe, who captured Roman metalsmiths and apparently put them to work. Archaeologists have found locally made Roman-style metal objects, such as statuettes, drinking horns and weapons, as far north as Denmark.

Captives could also change the religious practices of their captors' society. On the Northwest Coast of North America, Haida people learned from their Bella Bella captives about ceremonial gatherings called potlatches that were organized to build or repair a house. The people of Ouidah, a West African coastal slaving port, practiced a variety of vodun cults in the 19th century, some of which were introduced by slave women taken from interior African groups. And Germanic tribes who attacked the Roman Empire during its decline learned Christianity from Roman captives.

Although captors typically disdained their captives, they often believed they had curing powers. Spaniard Álvar Núñez Cabeza de Vaca was exploring the Gulf Coast a few decades after Columbus's voyage when he and several companions were shipwrecked and taken by native groups in what is now Texas. Their captors were sure these foreigners knew how to cure illness, and Cabeza de Vaca and his group became widely known for the healing ceremonies they invented. When the Spaniards escaped and made their way to what is now Mexico, the many native peoples they encountered along the way requested their skills as healers. Similarly, in the mid-19th-century American West, a wounded Oglala Sioux chief demanded his captive, a young pioneer woman named Fanny Kelly, attend him because he believed a white woman's touch would cure him. And in the Northeast region of North America, Huron captives are thought to have introduced the medicinal False Face Society, in which curers wore wood masks, to their Iroquois captors.

MUSEUM OF ANTHROPOLOGY, UNIVERSITY OF BRITISH COLUMBIA (*1*); JOSE ANTONIO CARRERA MUNOZ (*2*); WERNER FORMAN *Getty Images* (*3*)

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STATUS SYMBOLS

PERHAPS THE MOST SURPRISING finding from my study is that captives were a potent source of social and political power for their captors. In small-scale societies, social power stemmed from the number of followers a leader controlled, most of whom were relatives. However unwillingly, captives added significant numbers of nonkin followers and thus increased the status of their captors. Captives, especially women of reproductive age, allowed leaders or status-seeking men to increase the size of their family or number of followers without incurring the traditional marriage obligation of paying a bride price to the bride's family. And by definition, captives created instant inequality in the societies they joined. As the most marginal and despised members of the group, they raised everyone else's standing.

OLIVE OATMAN was kidnapped in 1851 by a Native American tribe in Arizona.

In most of the small-scale societies I examined, men gained prestige through success in war. Captives were the best evidence of victory. Among the Kalinago, for instance, a man could only achieve an advantageous marriage into a high-ranking family if he triumphed in war, which meant taking captives. Young Iroquois men in the Northeast region of North America could not expect to become leaders or marry well unless they were successful warriors—again, signified by captive taking. Men in societies throughout the Northeast used the "calumet ceremony," an alliance-building ritual that revolved around smoking sacred pipes, to boast of their success as warriors and captors. During the ceremony each warrior recounted the battles he had participated in and described every slave he had obtained. In the Philippine chiefdoms of Southeast Asia during the 12th through the 16th centuries, those warriors who took the most captives and the most booty during raids earned the highest status. They aspired to the successes of mythical warriors whose supernatural powers allowed them to overcome enemies and make off with their people.

Masters also attained social status through the public display of their power over their slaves. The stark disparity in daily routines between masters and captives constantly reinforced their relative standing. In this sense, high social status required not only master and servant but an audience to bear witness to the domination. Patterson has noted that the cult of chivalry of the American South, which emphasized the "honor" of Southern men, was only possible because white men could contrast themselves with powerless and, in their eyes, "honorless" slaves (regardless of whether they actually owned slaves). Similar dynamics played out in small-scale societies. For example, prominent Northwest Coast men called titleholders displayed their prestige in day-to-day interactions with their slaves. Titleholders performed only administrative tasks such as organizing ceremonial events and almost never did real work—the duty of slaves. Titleholder wives and daughters eschewed work, too. Slaves followed them everywhere to fetch wood and water, cook, carry burdens and mind children.

Among the Conibo, captives could also become retainers—household servants to high-ranking individuals or families—further elevating the social status of their masters. Likewise the Makú captives of the eastern Tukano people who inhabited the Vaupés River Basin of Brazil and Colombia cared for their master's personal needs and those of his wife. They held their master's large ceremonial cigar when he smoked and even breastfed their mistress's babies, according to anthropologist Fernando Santos-Granero of the Smithsonian Tropical Research Institute in Panama. Yet the Tukano scorned the Makú. Men might take Makú women as concubines but would never consider marrying one.

WEALTH BUILDERS

SCHOLARS HAVE ARGUED that slaves in small-scale societies were only status symbols with no real economic role. They have drawn a sharp contrast between this kind of slavery and large-scale slavery, the economic impact of which is evident from recent history: African slaves produced the wealth of the American South, a driving force in 19th-century American economic development. But the groups I studied suggest that captives in ancient smaller-scale societies actually began the process of creating the wealth, status and inequality that presaged the economic consequences of large-scale slavery in the U.S., Rome and elsewhere.

Leaders had to reward voluntary followers to maintain their loyalty, so their power was tied to their ability to control and provide food or items for trade. In small-scale societies, an aspiring leader generally turned to his kin to create the surplus he needed to gain and retain followers, but kin could reject the demand of the would-be leader. Powerless captives, of course, could not.

Precolonial examples of the economic impact of captives abound in the literature. Consider the 16th-century chiefdoms in the Cauca Valley of Colombia, which were constantly at war. The earliest Spanish visitors—soldiers and priests—reported that victors took hundreds of captives. They sacrificed some but kept many more as slaves, which allowed each master to significantly expand his crop production. On North America's Northwest Coast, salmon was a dietary staple for many groups, but it was available only at certain times of the year, so people had to preserve it for storage. The tribes considered salmon processing women's work. But they readily set slaves of both sexes to this task, which created surpluses of dried salmon. Elsewhere in North America, on the

BENJAMIN F. POWELSON *Alamy*

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Great Plains in the century before Europeans arrived, men became wealthy through the production and trade of high-status bison robes and hides. Producing hides and robes was labor-intensive women's work. Archaeologist Judith Habicht-Mauche of the University of California, Santa Cruz, has found evidence that Plains men captured women from Pueblo Indian villages to increase their numbers of wives. Remains of pottery made in the Plains using techniques associated with Pueblo culture track the movement of these Pueblo women into Plains groups. Cooperative work among many wives could double hide production and significantly increase a man's wealth and status, Habicht-Mauche contends.

The resources generated by captives allowed chiefs and aspiring leaders to sidestep reciprocal obligations to kin and to consolidate their social and economic power. In the Philippines, captive women produced food, textiles or pottery. Chiefs used the surplus goods to sponsor feasts that attracted warriors to follow and fight for them, thus growing their armies; would-be chiefs, meanwhile, traded the goods throughout Southeast Asia to build their wealth. The Conibo of Peru had a similar means of converting the surplus wealth generated by captives into power and status—namely, the "competitive feast." According to archaeologist Warren DeBoer of Queens College, C.U.N.Y., an authority on the Conibo, it was important for ambitious Conibo men to have multiple wives helping with the feast. Both traditional and captive wives farmed the staple manioc and brewed it into beer, the centerpiece of competitive feasts. The more wives a man had—and successful raids of the small villages upriver yielded a steady supply—the more beer his household produced. The more beer he could offer, the bigger the feast he could hold and the greater his standing. This dynamic appears to have deep roots: discoveries of first-millennium pots for brewing, storing and drinking beer suggest that competitive feasting, and most likely the captive women who supported it, were common among the prehistoric ancestors of the Conibo and many other ancient societies.

Captives not only produced wealth, they literally embodied it. Virtually all the small-scale societies I studied gifted, traded or sold stolen people. As was true in the slavery system of the American South, low-status captives were high-status prestige goods and often the most valuable commodities men in small-scale societies owned. In the Northeast region of North America in the 17th and 18th centuries, indigenous groups used captives as gifts to create alliances or smooth over disputes. On the Northwest Coast, slaves were exchanged or sold from group to group, moving along well-established trade routes. In Colombia's Cauca Valley, the oldest known explorers' accounts, from the mid-1500s, describe slave markets—an institution that very likely predated European contact. In some parts of the world, slaves even functioned like money. In early medieval Ireland, for instance, the female slave was the highest unit of value and was used as a method of payment.

FROM TRIBE TO STATE

GIVEN THE IMPACTS of captives on the cultures they entered, I suspect they played an important role in one of the fundamental social transitions in human history: the formation of complex, state-level societies. Archaeologist Norman Yoffee, now at New York University, has argued that state-level societies did not emerge until socioeconomic and governmental positions were no longer linked to kinship. And most archaeologists and other social scientists agree that states were at least in part the result of a few people creating and controlling surplus goods. Captive taking helped early human groups meet both these conditions for the evolution of statehood. Captives were not the only factor in the formation of states, of course. They existed in many small-scale societies around the world without effecting this dramatic social change. But captives were (and still are) taken to bolster the social status of ambitious men and, in my view, gave some of these men the opportunity to accrue the quantities of wealth and power that must have been the foundation of early states.

If captive taking was involved in the formation of state-level societies, then we should expect to find signs of captives among the remains of early states. Exactly such evidence has come from one of the places that I have worked at in the American Southwest, New Mexico's Chaco Canyon. The Chaco polity existed from around A.D. 800 to 1250 and has been argued to be the only state-level society in the Southwest. Studies of human remains have revealed significantly more females in the surrounding area in the period during which Chaco was in power compared with when it was not. Burials from Chaco Canyon itself contained many women ages 15 to 25, the most common sex and age range for captives. In addition, a study of human remains from a Chaco-style great house near Chaco Canyon found women with evidence of healed head wounds and other trauma of the kind often associated with captives and other marginalized and abused people. Other evidence of violence in the Chaco region, as well as oral traditions among the modern-day descendants of the Chacoans, also attests to the presence of captives in Chaco.

Chaco is not the only example. Archaeologist Peter Robertshaw of California State University, San Bernardino, examined the development of two East African states, Bunyoro and Buganda, after the mid-15th century, in what is now western Uganda. He found that many of the women who worked in the banana or millet fields there had been captured and were treated as commodities. Demand for women's agricultural labor may have been the motor of sociopolitical evolution of these societies, Robertshaw suggested.

The notion that captives contributed to sociopolitical change that ultimately gave rise to the modern world does not in any way justify the egregious mistreatment of captives in ancient, historical or modern times. More than five years after ISIS forces ravaged their homeland, some of the Yazidi women and children they enslaved have returned home. Thousands remain in captivity. I fervently hope that more Yazidi captives will be reunited with their families. Women in such situations through the millennia almost never had such hope. Archaeologists can, at least to some small degree, acknowledge and honor their plight by telling their stories. SA

Catherine M. Cameron is an archaeologist at the University of Colorado Boulder. Her work focuses on sites in the American Southwest, including Chaco Canyon. She has been studying captives in early small-scale societies around the world for the past 12 years.

MORE TO EXPLORE

The Creation of Inequality: How Our Prehistoric Ancestors Set the Stage for Monarchy, Slavery, and Empire. Kent Flannery and Joyce Marcus. Harvard University Press, 2012.

Captives: How Stolen People Changed the World. Catherine M. Cameron. University of Nebraska Press, 2016.

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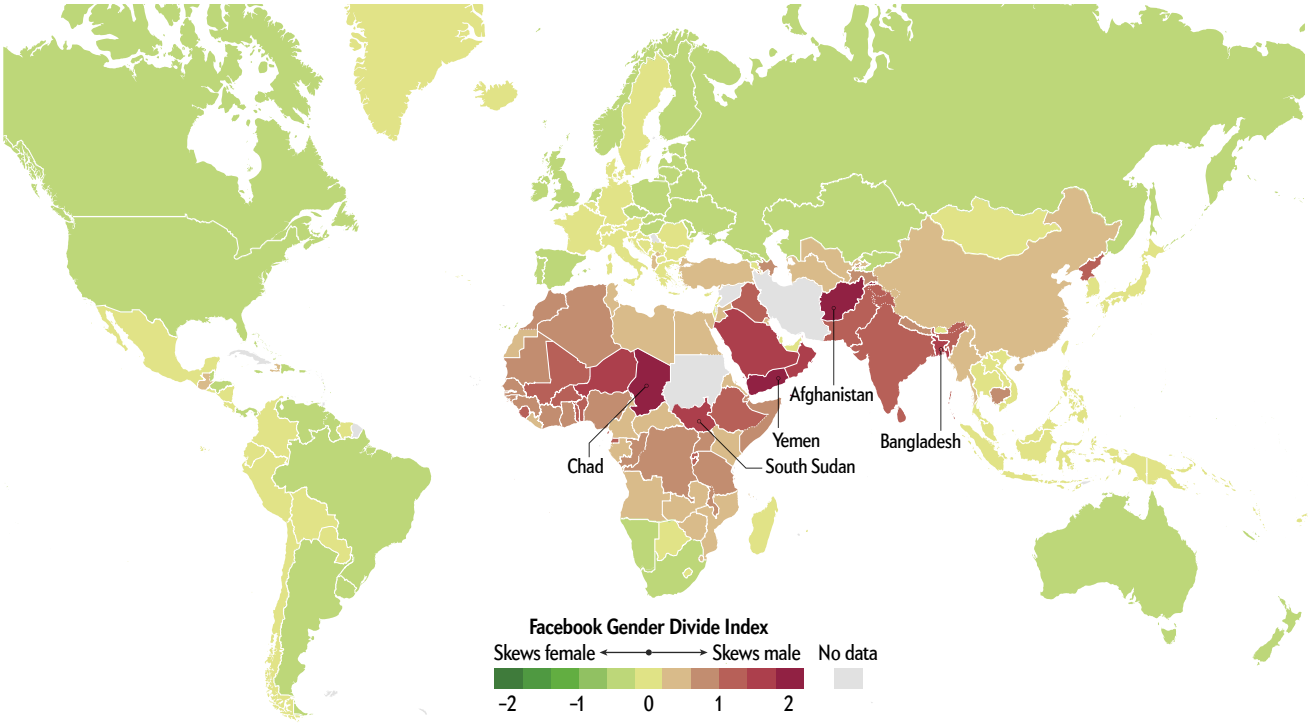
The Facebook Gender Divide around the World



THE FACEBOOK GENDER GAP

Social network use may be a valuable metric for equality

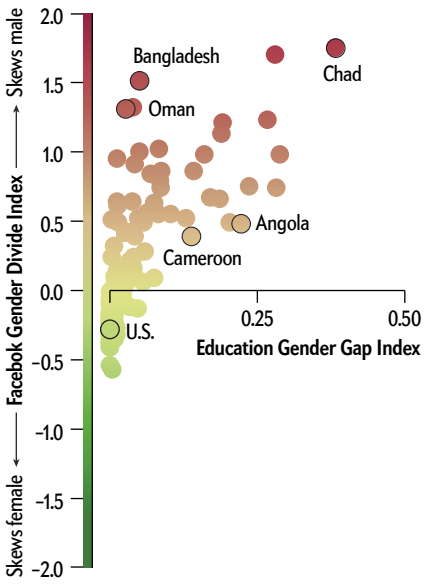
By Matthew Hutson

In addition to purveying cat videos and baby pictures, social networks can provide useful demographic information. A recent study finds that worldwide, Facebook use by women is associated with greater gender equality.

Researchers looked at the anonymized data of 1.4 billion users in 217 countries, territories and autonomous regions and calculated the proportion of women and men ages 13 to 65 who actively used the social network. Places with a lower female-to-male usage ratio, such as Afghanistan, were deemed to have a greater "Facebook gender divide" (*chart* and *map*). The team also collected World Economic Forum data on countries' gender equality in terms of economic opportunity, education and health. The study found that the smaller a country's Facebook gender divide in 2015, the more economic gender equality increased the following year. In contrast, an increase in economic gender equality in 2015 was not associated with a reduction in the Facebook gender divide during 2016. This finding suggests that a smaller Facebook gender gap is more likely a contributor to—rather than a result of—economic gender equality. The results were published in July 2018 in the *Proceedings of the National Academy of Sciences USA*.

Ridhi Kashyap, a demographer at the University of Oxford, who was not involved in the study, has published a separate map of the Internet gender gap, also using Facebook data. She found that gender gaps in Facebook use proved to be a good measure of gender gaps in Internet use in general; data on the latter are often unavailable. Kashyap says the Internet can provide users with valuable health and employment information and "can also be a great way to enhance skills." David Garcia, a computational social scientist at the Medical University of Vienna and the lead author of the *PNAS* study, says Facebook data could help policy makers estimate gender inequality in poor countries and could track its evolution on a daily basis.

The Facebook Gender Divide vs. the Education Gap



SOURCES: "ANALYZING GENDER INEQUALITY THROUGH LARGE-SCALE FACEBOOK ADVERTISING DATA," BY DAVID GARCIA ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 115, NO. 27; JULY 3, 2018 (*Facebook gender divide data*); THE GLOBAL GENDER GAP REPORT 2016, WORLD ECONOMIC FORUM, 2016 (*education gender gap data*)

Matthew Hutson is a freelance science writer based in New York City and author of *The 7 Laws of Magical Thinking* (Penguin Group USA, 2012).

Graphics by Amanda Montañez

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INDIA HAS A FEMALE SUICIDE CRISIS

The high rate may be driven by a disconnect between ambition and social acceptance

By Dana G. Smith

Women in India are committing suicide at an alarming rate. Research published in the October 2018 issue of the *Lancet Public Health* reveals that in 2016 they accounted for more than 36 percent of female suicide deaths globally, despite making up less than 18 percent of the world's female population. Suicide is the leading cause of death among Indian women ages 15 to 29, responsible for about 26 to 33 deaths per 100,000 women in that range. According to the Global Health Data Exchange, a database that tracks worldwide health trends and demographics, India has the highest suicide rate among young and middle-aged women for countries with similar sociodemographics.

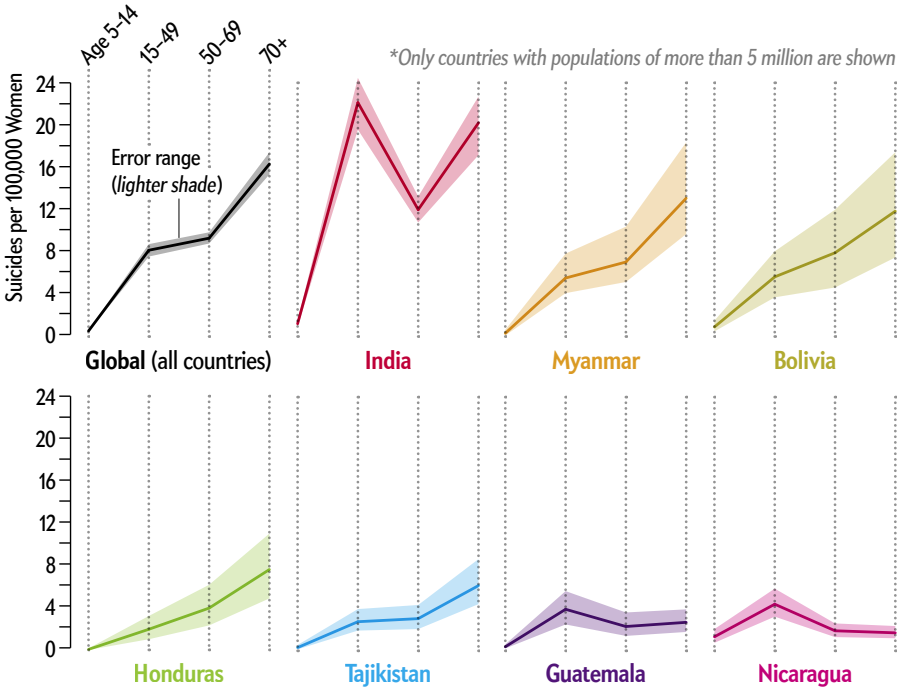
The situation may be related to a clash between women's aspirations and the rigidity of their social environment, hypothesizes study author Rakhi Dandona, a professor of global health at the Public Health Foundation of India and the University of Washington. As India has developed, women have become better educated and more empowered, and arranged marriages have declined. Yet in many aspects of society, women still possess lower status and face barriers to opportunity. Dandona and other experts suspect this disconnect may drive some to despair. Suicide rates are especially high in southern Indian states, where development and social advances have accelerated. In contrast, Dandona says, suicide rates in the rural, more traditional northern states could be lower because women there may have "less knowledge that they could actually live a better life."

"Deaths that occur due to suicide are also a product of the method that is used," says Vikram Patel, a professor of global health at Harvard University, who was not involved in the *Lancet Public Health* study. In the West, women attempt suicide more often than men, but men typically use more lethal means, resulting in more deaths. In India, however, Patel says that men and women tend to use the same, more fatal, methods.

Dana G. Smith is a freelance science writer specializing in brains and bodies. She has written for *Scientific American*, the *Atlantic*, the *Guardian*, NPR, *Discover*, and *Fast Company*, among other outlets.

National suicide rates are typically linked with a country's sociodemographic index (SDI)—a measure of development derived from average income, educational attainment and fertility rate. Based on India's SDI, researchers found that the suicide rate among women there was almost three times higher than expected. Moreover, whereas suicide rates often increase with age, Indian women between 15 and 49 die from self-harm at a rate exceeding that of all other age groups. The graphs compare suicide rates by age group in countries with almost exactly the same SDI as India's. To avoid potential statistical anomalies, countries with populations of fewer than five million are excluded.

Suicide Rates among Women in India and Sociodemographically Comparable Countries, 2016*



SOURCE: GLOBAL HEALTH DATA EXCHANGE

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Return of the Missing Daughters

Traditions that favor sons in Asia—resulting in millions of dead or neglected girls—have started to change

By Monica Das Gupta

Illustration by María Corte

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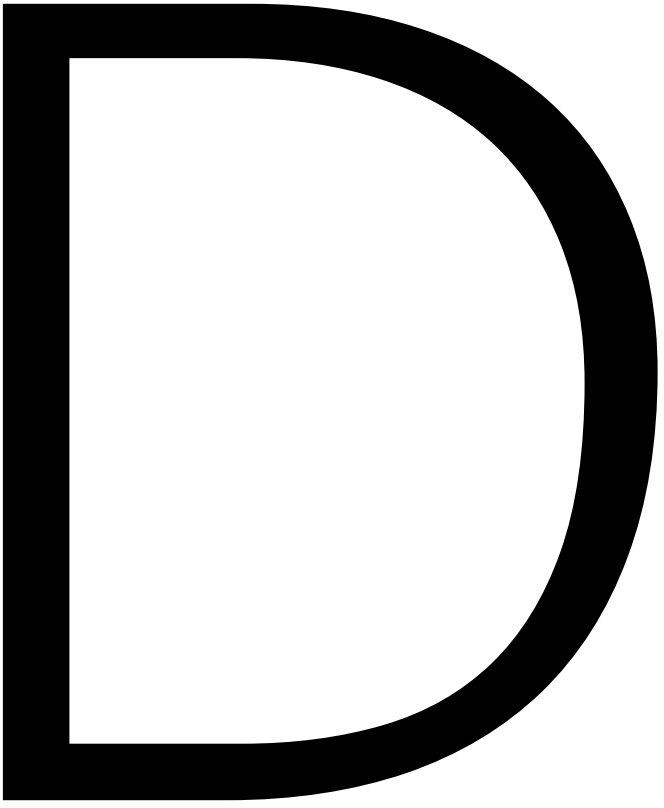

AUGHTERS ARE USELESS AND UNWORTHY!" shouted an elderly woman in a village near Busan in South Korea in 1996. Other old women sitting with her, as we talked about families, nodded their agreement. Why, I asked? It was not because daughters were lazy, she said. "No, women did a lot of hard labor in the fields, and their marriage costs virtually nothing. People don't want daughters, because they are not helpful to the family—they leave the family when they marry. It is *sons* who stay home, inherit assets and keep the rituals of ancestor worship."

IN BRIEF

Until very recently, many cultures in Asia and elsewhere have valued boys more than girls, and female children were often killed or neglected by their families.

Generations of missing women have been harmed, and their absence has hurt societies, altering marriage patterns and migration in and out of regions and countries.

Now more gender equality is starting to take hold, and as cultures grant more economic value to women, birth ratios no longer favor sons so heavily.

In China, I heard similar stories. A man said that when his daughter was born, "my wife was so upset that she did not want to care for the child, and I had to persuade her to nurse it."

These attitudes have had life-and-death effects. The natural human male-female birth ratio is only about 5 to 6 percent more boys than girls. But in China in 2000, there were 20 percent more boys born. This kind of skewed sex ratio has been found across much of East Asia, South Asia, the southern Caucasus and parts of the Balkans. Female babies are aborted in these areas, killed at birth or die through neglect. Why? As the woman from Busan said, it is brutal economics. These cultures have historically excluded adult daughters from helping in their parents' households or inheriting property, which diminishes their value to their birth family.

But recently the demographic bias against females has begun to shift. South Korea has shown a rebalancing of child sex ratios since the mid-1990s, with proportions of boys to girls dropping from high levels to biologically normal ones. There is even a shift toward a preference for daughters in South Korea today. In India, the 2011 census shows a sharp drop in sex ratios in children in the northwestern part of the country, where they had been very high. In China, the climb in such sex ratios has leveled off.

These shifts coincide with rapid urbanization and social changes that have helped make daughters more valuable to their parents. Daughters no longer vanish from their birth families, and in some cases, they bring in additional men from outside. Twenty years after my original fieldwork in Busan, one woman in South Korea told me, "My mother suffered a lot of abuse when she was young because she had three daughters and no sons. Now that we are grown, she is very happy because we all remain close to her. She says that her sons-in-law treat her better than sons."

SHOVING WOMEN OUT

FOR CENTURIES the social organization of rural society in China, South Korea and northwestern India pushed daughters away from their parents' households. When women married, they were absorbed into their husband's family. New labor in their birth family was provided by daughters-in-law marrying in, further emphasizing the value of sons. A similar social structure appears in other regions with strong son

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preference, including northern Vietnam and the southern Caucasus countries.

To cement this daughter transfer, when a woman joins her husband's family, her "slot" in her birth family is eliminated. A new slot is created for incoming brides. If women do return—a rare occurrence—they and their parents have to struggle hard to make the unusual situation work. Other members of the family and the village resist because of the potential reduction of their property rights. Once a woman from rural China has been married and her land entitlement reallocated among village residents, for example, her return can be met with a fair amount of antagonism.

The impact of these cultural norms can be seen in the contrast between elder living arrangements in countries such as Taiwan and South Korea and those in countries such as the Philippines. The first two have rigidly patrilineal (male-oriented) kinship systems, whereas the third has a system of kinship that does not favor children of any one gender. In Taiwan and South Korea, a substantial proportion of parents live with married sons, but almost none live with married daughters, according to a study I conducted with Doo-Sub Kim of Hanyang University in Seoul and our colleagues. In the Philippines, parents are equally likely to live with married children of either gender. It is not surprising that child sex ratios are normal in the Philippines but have been lopsided in Taiwan and South Korea.

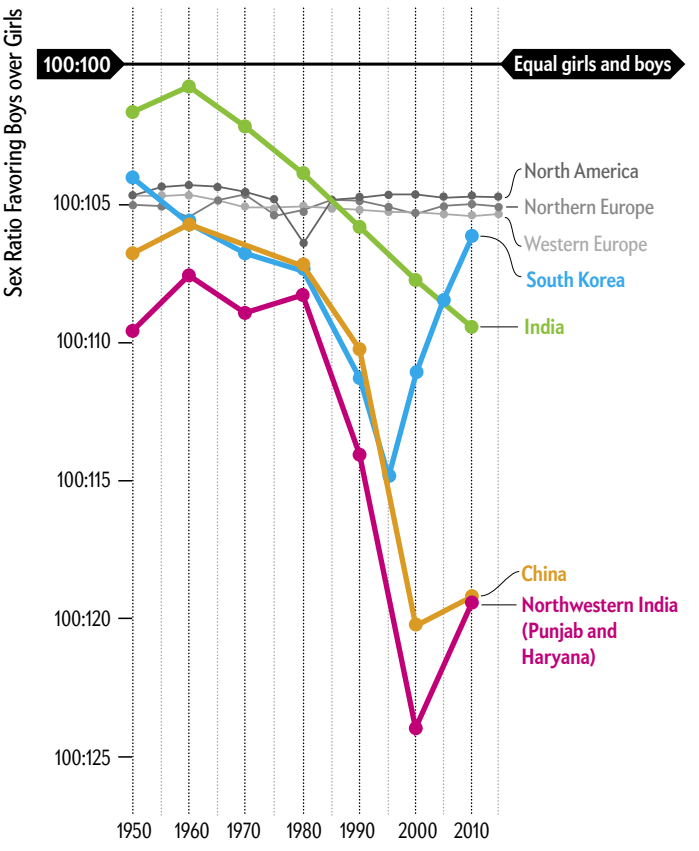
The results of devaluation of females are not surprising, either. Unwanted girls have been removed through infanticide and neglect, producing male-skewed child sex ratios. Beginning in the 1980s, sonograms and other technologies for prenatal sex detection made it possible to act on sex bias even before birth. The new methods made it easier for parents to avoid having unwanted daughters—through abortion—and sex ratios at birth showed more imbalance.

Major disruptions such as famine and war heighten the pressure on parents to get rid of children they perceive to be superfluous. Beginning in 1937, Japanese troops swept through eastern China, and girls went "missing:" 17 percent more girls died than one would expect from typical mortality rates in this situation. Parents in war-torn regions felt that they had to make some harsh choices. A woman in the province of Zhejiang told me of her own experience in the 1930s: "When I was six years old, my mother said that I should be sold. I begged my father not to do this, that I would eat very little if only they would let me stay at home." The collapse of governmental institutions can have similar effects. In the southern Caucasus countries, for instance, birth ratios favoring boys shot up when the U.S.S.R. was dissolved.

A shift from large to small family size also increases the pressure on parents to select for sons. In large-family, high-fertility settings, parents can afford to have several daughters and still go on to have one or two sons. In small families with fewer births, there are only limited chances to have sons. The second girl born into such families in son-favoring cultures has a much higher chance of dying before birth or during early childhood.

Different Places and Losses

South Korea, China and northwestern India lost many girls during the 20th century—victims of infanticide or neglect in patriarchal cultures. Census data and population surveys show drops in the numbers of girl babies and young children, compared with those of boys. The effect was not seen in Europe and North America. Recently cultural values have changed, and girls have rebounded.



WHEN BRIDES ARE IN SHORT SUPPLY

THE DEATHS of these female babies are a shocking result of gender inequality. The damaging effects ripple through society. Eventually they translate into a shortage of adult women. And after heightened periods of sex selection in earlier decades, a "marriage squeeze" now grips China, South Korea and northwestern India. China presents the starkest scenario. In 2010 the Chinese Academy of Social Sciences estimated that by 2020, one in five men in China will be unable to find a wife.

The bride shortage affects poorer men most se-

SOURCES: "'MISSING GIRLS' IN CHINA AND INDIA: TRENDS AND POLICY CHALLENGES," BY GUO ZHEN, MONICA DAS GUPTA AND LI SHUZHUO, IN *ASIAN POPULATION STUDIES*, VOL. 12, NO. 2. PUBLISHED ONLINE JUNE 6, 2016 (*children in India, ages 0–6, and children in South Korea and China, ages 0–4*); NATIONAL CENSUS DATA (*China, India, South Korea*); *WORLD POPULATION PROSPECTS: THE 2017 REVISION*, DVD EDITION, POPULATION DIVISION, DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS, UNITED NATIONS, 2017 (*North America, Western Europe, Northern Europe*)

Graphics by Jen Christiansen

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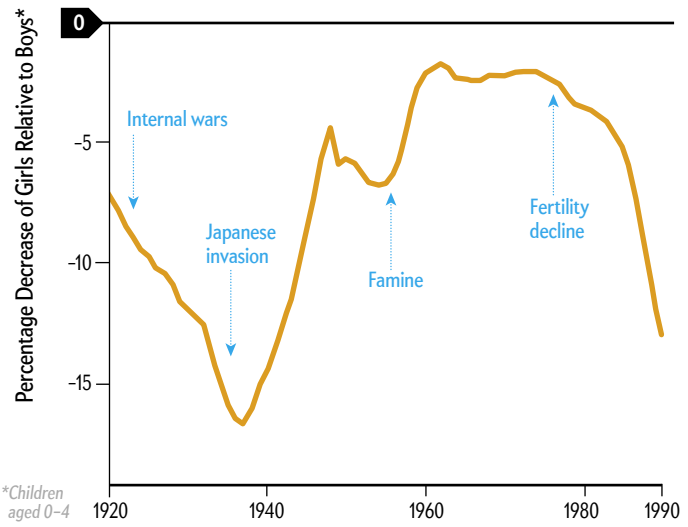
In Hard Times, Girls Suffer

In China, the numbers of girls have dropped, compared with what would be biologically normal, during difficult times. Families jettisoned less valued female children during internal wars in the 1920s, a Japanese invasion in the late 1930s, famine in the 1950s and pressure to have small families in the 1980s.



verely. In China, Shang-Jin Wei of Columbia University and his colleague report that poorer parents in areas with imbalanced sex ratios struggle to improve their sons' chances in the marriage market. The parents resort to desperate measures such as taking on dangerous work to earn more and build a nicer house, one that can attract this newly scarce and valuable commodity: a bride to marry into the family.

At the same time, the marriage squeeze can benefit women. In areas of China with fewer potential brides, a study by Maria Porter of Michigan State University found that women have greater bargaining power within their marriage, enabling them to provide greater support for their parents than before. Women from poor areas can marry men who offer higher living standards, either locally or by migrating to other parts of their country. Some migrate to other countries to marry better-off men. In China, South Korea and India, several studies show these long-distance suitors are typically socioeconomically disadvantaged compared with other men in their own locale. They are unable to attract a local wife but still can offer an improved standard of living to women from impoverished regions. These migration marriages do come with risks for women, however. Some research suggests that women who come from different ethnic or linguistic groups face problems in assimilation, are viewed as outsiders, do not know the local language and customs, and have limited social networks in their new setting. Many such marriages are to men who live in rural areas, and rural life further isolates the brides.

Difficulties can go beyond social isolation and cultural misunderstandings. In a 2010 study of Vietnamese brides in Taiwan, done by researchers at Vietnam National University, Ho Chi Minh City, most women said that they were happy because they were able to help their birth families financially. But some mentioned problems, such as being humiliated by their husband and in-laws for their poverty, suffering domestic violence or being made to work like a slave. In Taiwan, in fact, a 2006 study found that marriage migration was a risk factor in domestic violence. And in South Korea, Hanyang's Kim found a greater likelihood of divorce among such marriages.

Some researchers and policy makers have also suggested that the creation of a generation of enforced bachelors may raise levels of crime and violence, including violence against women. Crime levels climbed in areas with higher male-to-female ratios, according to a study in India led by Jean Drèze, now at the University of Allahabad, as well as another study, which was conducted in China by Lena Edlund of Columbia and her colleagues.

THE VALUE OF WOMEN

OVER THE PAST TWO DECADES the bias against girls has begun to diminish. My colleague Woojin Chung and I documented this phenomenon in a study of South Korean women's changing attitudes toward children's gender. When interviewed in 1991, 35 percent of women born between 1955 and 1964 said that they "must have a son." But by 2003, only 19 percent of women born in that same period held this view. Changes in attitude have swept across society. Even after accounting for differences in education levels and urban versus rural residence, the odds of women aged 15 to 49 stating they "must have a son" in 2003 were roughly one third of the 1991 level. Changes in social norms account for as much as 73 percent of this decline. Only 27 percent of the drop is caused solely by increases in individual levels of education and urbanization. When attitudes changed, child sex ratios followed, as shown in the box on the opposite page.

WHAT TURNED THE CORNER, ENHANCING GIRLS' VALUE? IT IS HARD TO TEASE OUT, BUT INCREASING URBANIZATION AND EDUCATION OF PARENTS PLAY A MAJOR ROLE.

SOURCE: "GENDER BIAS IN CHINA, SOUTH KOREA AND INDIA 1920–1990: EFFECTS OF WAR, FAMINE AND FERTILITY DECLINE," BY MONICA DAS GUPTA AND LI SHUZHUO, IN *DEVELOPMENT AND CHANGE*, VOL. 30, NO. 3, JULY 1999

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What turned the corner, enhancing girls' value? It is a hard answer to tease out, but the increasing urbanization and education of parents play a major role. South Korea, for example, has urbanized at blistering speed, with the percentage of people living in and around cities doubling between 1966 and 1986, from 33 to 67 percent. By 1991, 75 percent of the population lived in urban areas. The effects of urban life on son preference are both social and economic. Living in a city reduces the centrality of sons' roles in their parents' lives. While villagers spend their days surrounded by clan members, urban residents live and work in the more impersonal settings of apartment blocks and office complexes. This shift relieves pressure to conform to traditional expectations of filial duty and to have sons to continue the lineage.

In urban areas, children who support their parents tend to do so less because of formal rules and more because they happen to live in the same city and have strong relationships with their parents. In this way, urbanization helps to bridge the gap between the value placed on daughters and sons. Female education and employment also enhance the potential support they can offer. And with growing access to pensions and social protection systems, people become less dependent on their children for financial support.

Government policies have also nudged male preference into decline by encouraging mainstream equality for women. India has used affirmative action to increase women's political participation, putting a female quota in place for candidates for local government positions. Social scientists have found that after the policy was created, gender stereotypes weakened in the population as a whole, and girls' aspirations for themselves rose.

Extensive media outreach has also been a staple feature of family-planning programs in India, China and South Korea. Posters and commercials encourage parents to have small families even if they do not include sons. These efforts promote the view that daughters are just as good as sons for family happiness.

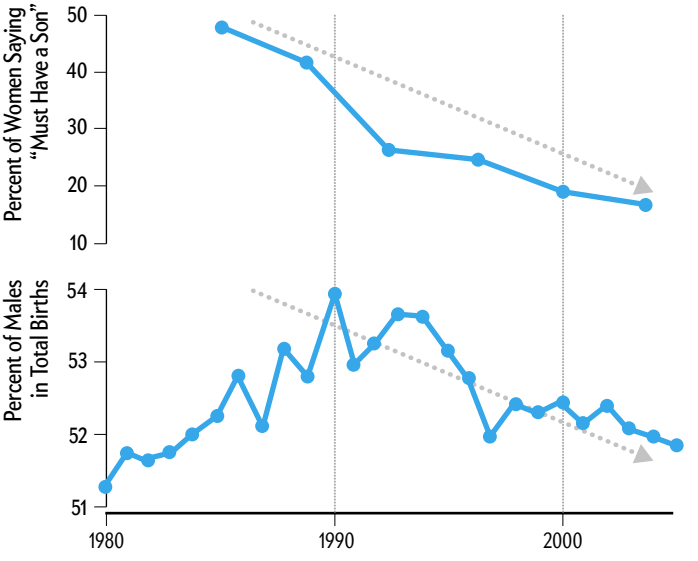
Female characters portrayed in popular Indian television soap operas now work outside the home and are active in public life. The values and roles that are illustrated in these programs challenge traditional views of a woman's place in society. Studies show that exposure to these messages is associated with reduced son preference.

There have also been direct attempts to change sex ratios by banning the use of technology for prenatal sex detection and selection. These bans have been put into place in several countries, but there has been little rigorous evaluation of the impact of these measures because of a lack of data. India's ban on sex selection appears to have had at most a modest effect. A vigorous effort in China to ban birth selection has shown little effect on the national sex ratio of babies.

Countries in Asia are still urbanizing rapidly, so I believe the preference for sons will continue to decline. Policy makers can accelerate this process through legal and other measures enhancing gender equity. They can also expand media advocacy and portray women helping their own aging parents (not just their in-laws). Such steps help to change gender stereotypes and overcome parents' preference for sons. For women—and for society in general—such approaches may have better outcomes than outright attempts to ban the selection of sex at birth. SA

Sex Ratios Follow Social Preference

In South Korea, the stated desire for sons instead of daughters dropped sharply by the early 1990s. The actual percentage of sons born began falling soon after that, showing the power of changing values.



SOURCE: "THE DECLINE OF SON PREFERENCE IN SOUTH KOREA: THE ROLES OF DEVELOPMENT AND PUBLIC POLICY," BY WOOJIN CHUNG AND MONICA DAS GUPTA, IN *POPULATION AND DEVELOPMENT REVIEW*, VOL. 33, NO. 4; DECEMBER 2007; NATIONAL CENSUS DATA

Monica Das Gupta is a research professor at the University of Maryland's sociology department and is a former senior demographer for the World Bank.

MORE TO EXPLORE

Gender Bias in China, South Korea and India 1920–1990: Effects of War, Famine and Fertility Decline. Monica Das Gupta and Li Shuzhuo in *Development and Change,* Vol. 30, No. 3, pages 619–652; July 1999.

Why Is Son Preference So Persistent in East and South Asia? A Cross-Country Study of China, India and the Republic of Korea. Monica Das Gupta et al. in *Journal of Development Studies,* Vol. 40, No. 2, pages 153–187; 2003.

Crisis of Masculinity in Haryana: The Unmarried, the Unemployed and the Aged. Prem Chowdhry in *Economic and Political Weekly,* Vol. 40, No. 49, pages 5189–5198; December 3–9, 2005.

The Decline of Son Preference in South Korea: The Roles of Development and Public Policy. Woojin Chung and Monica Das Gupta in *Population and Development Review,* Vol. 33, No. 4, pages 757–783; December 2007.

Sex Ratios and Crime: Evidence from China. Lena Edlund et al. in *Review of Economics and Statistics,* Vol. 95, No. 5, pages 1520–1534; December 2013.

"Missing Girls" in China and India: Trends and Policy Challenges. Guo Zhen, Monica Das Gupta and Li Shuzhuo in *Asian Population Studies,* Vol. 12, No. 2, pages 135–155. Published online June 6, 2016.

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WHEN TIMES ARE GOOD, THE GENDER GAP GROWS

A study shows growing national wealth and gender equality accentuate differences in the types of choices women and men make

By Emily Willingham

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AS THE ECONOMY IMPROVES and gender equality increases, women in the workforce appear to make increasingly different social choices than men do.

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IN AN IDEALIZED VERSION OF HUMAN EXISTENCE, WEALTH LIFTS ALL BOATS, gender equality prevails and everyone behaves freely as the individuals they are. Such a gender-equal fictional utopia starts from a premise that equal access to wealth and opportunity will erase the divide between men and women. But what if the utopian predictions are wrong? What if women and men, when all other things are largely equal, express more, not less, of a gender-based perspective? Armin Falk, an economics professor at the University of Bonn in Germany, and Johannes Hermle, a doctoral student in economics at the University of California, Berkeley, have undertaken a massive study that looks worldwide at how national wealth and gender equality affect the choices men and women make when they think about risk taking, altruism and other social factors.

In their study, which involved 76 countries and 80,000 people, they found greater national wealth and gender equality are tied to bigger differences in preferences between men and women rather than to stronger similarities. They reported their results, which they say favor one of two competing hypotheses on gender choices, in October 2018 in *Science*. "This is important work that will have a lot of impact," says Matthias Doepke, an economics professor at Northwestern University, who was not involved in the study. But, he says, "the world is complicated, and I think we will find that neither hypothesis alone is a good summary of the data."

Those theories address how national wealth and equality affect the choices men and women make. One of them, which the authors dub the "social role hypothesis," predicts wealth and gender equality will lead to more similarities in preferences between genders. With equality and readily available resources, the idea goes, women and men will become more alike in their ways.

The "resource hypothesis," in contrast, holds that abundance and equality will give men and women more freedom to express gender-related preferences, unconstrained by hardships that might force them to do otherwise. In this scenario, a woman who worked in a male-dominated field 50 years ago might have felt pressured to behave as "one of the boys." But with a more equal gender representation in the workplace, perhaps such constraints would fade, leaving her freer to express more gendered preferences if she wishes.

To test these two ideas, Falk and Hermle used responses to a survey from people representing every continent and countries at every level of economic development. The Global Preferences Survey asked participants about how they would respond in different scenarios involving six social factors: risk taking, patience, altruism, trust, and positive and negative reciprocation (responding in kind to positive or negative interactions). For example, positive-reciprocity respondents had to settle on how much they would pay for a thank-you gift to a total stranger in return for a good deed. They also rated their responses to this statement: "When someone does me a favor, I am willing to return it." They were asked to rate their responses on a scale of 0 to 10, with 0 being not at all willing.

When the two researchers aligned these responses with the gross domestic product (GDP) for each country, they found higher GDP tracked with increasing differences in men's and women's preferences. When they mapped the survey responses against an index of gender equality in each country—based on factors such as when women gained the right to vote—they found again greater equality tracked with an increasing gender gap in preferences around trust, altruism and the other variables.

Falk and Hermle also batched GDP values into four groups to assess each of the six social factors separately. For all six, the two genders were much more similar in their preferences in the lowest compared with the highest GDP groups. The same pattern applied for gender equality: across four bins of gender-equality index values, the lowest values were associated with the smallest gender differences, the highest with the greatest gender differences in preferences. "Our study confirms the (resource) hypothesis," Hermle says. "The main takeaway is that gender differences in preferences are increasing with country level of economic development as well as gender equality."

Alessandra Fogli, monetary adviser in the research department at the Federal Reserve Bank of Minneapolis, who was not part of the study, sees a missed opportunity in the analysis. "I wish they had first discussed the variation of overall preferences across countries, such as how trust or risk aversion varies across income groups, and not just the differences across genders," she says. "The paper offers a suggestive, interesting finding to motivate a deeper, more systematic analysis. But I do not find it conclusive."

Doepke also expresses some uncertainty. "I think the contrast and evaluation of the social role and resource hypotheses is a bit too simplified," he says. "What should matter is the conditions when the respondents of the study were socialized." He points out that with survey participants ranging in age from adolescence to the 90s, socialization could have occurred decades ago for some, when gender divisions even in the richest economies "were very sharp." He adds that "gender-preference gaps among millennials would tell us something about how boys and girls were socialized in the past 25 years or so, whereas preference gaps for older cohorts would be informative on conditions in earlier times." Having more resources, he observes, might simply mean parents

Emily Willingham is a science writer and co-author, with Tara Haelle, of *The Informed Parent: A Science-Based Resource for Your Child's First Four Years* (TarcherPerigee, 2016). She writes about the intersection of brain research and society.

PRECEDING PAGES: GETTY IMAGES

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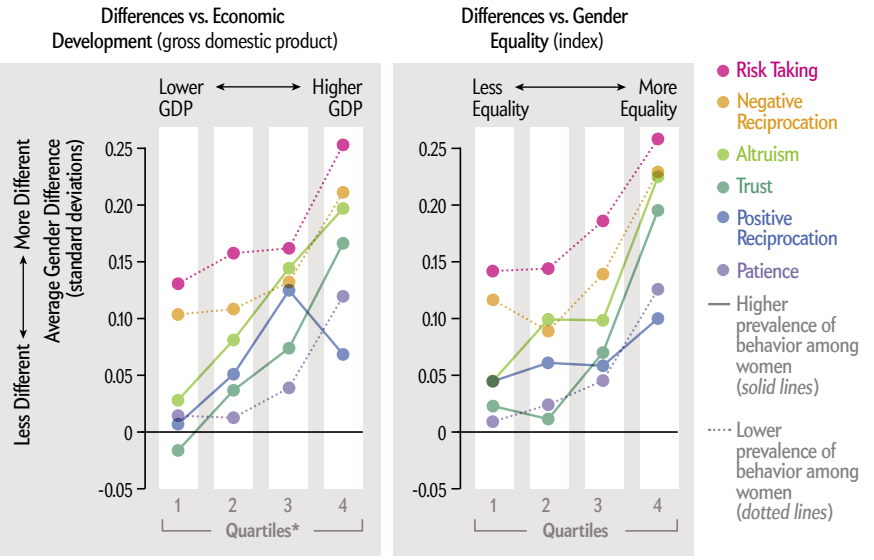
Equality's Effect on Choice

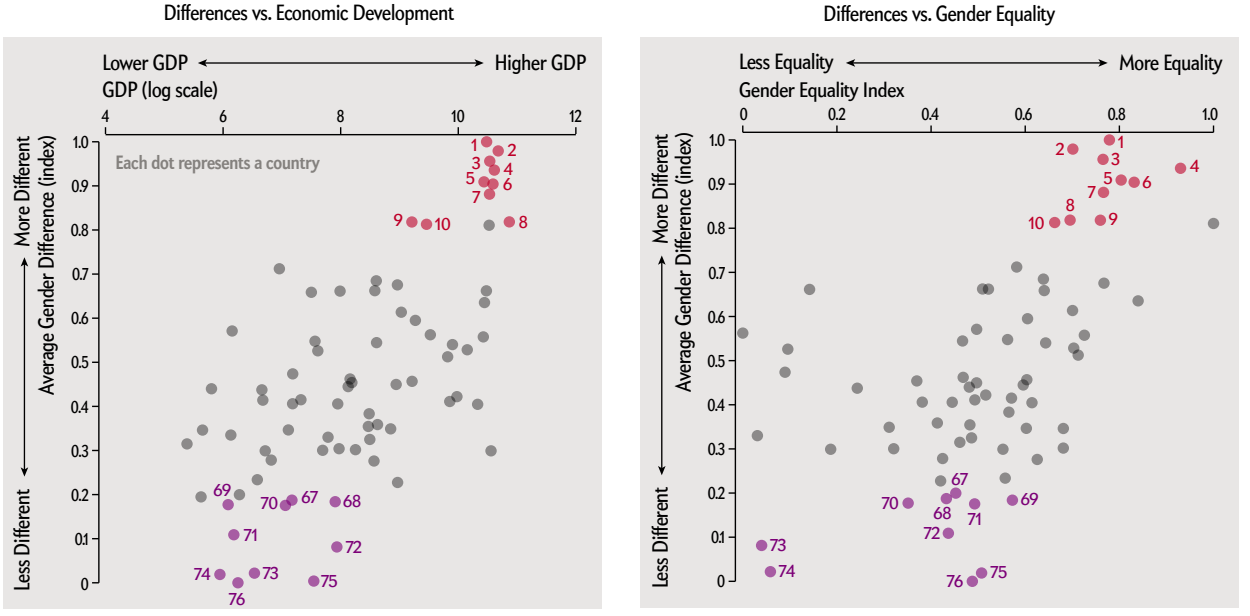
In countries where the economy thrives and gender inequality is declining, do women and men become more similar in the choices they make? Maybe not. A study of 80,000 people from 76 countries shows the more things get better, the more men and women differ in their choices related to social factors such as altruism and trust.

Gender Differences in Choices by Choice Type



*Quartiles refer to four equal groupings of GDP or index values, from lowest to highest, for the 76 countries studied.

Gender Differences in Choices by Country



Largest Gender Differences 1. Canada 2. U.S. 3. U.K. 4. Sweden 5. Australia 6. Netherlands 7. Austria 8. Switzerland 9. Estonia 10. Czech Republic
Smallest Gender Differences 67. Sri Lanka 68. Thailand 69. Bangladesh 70. Nicaragua 71. Cambodia 72. Iran 76. Ghana

SOURCE: "RELATIONSHIP OF GENDER DIFFERENCES IN PREFERENCES TO ECONOMIC DEVELOPMENT AND GENDER EQUALITY," BY ARMIN FALK AND JOHANNES HERMLE, IN *SCIENCE*, VOL. 362; OCTOBER 19, 2018

have more time to socialize their children in gender-specific ways.

According to Hermle, various explanations for the findings are plausible. These social roles "are very powerful in explaining gender differences and preferences," he says, but the current study did not measure such factors. Their analysis establishes a pattern that needs to be further examined to confirm or reject underlying causes, he notes.

Hermle also wants to ensure their findings are not misinterpreted as favoring evolutionary or biological explanations over social factors. "The biggest misinterpretation could be that our results indicate that social or gender-specific roles do not matter in the formation of gender differences in preferences," he says. "I do think that they matter a lot." SA

MORE TO EXPLORE

Relationship of Gender Differences in Preferences to Economic Development and Gender Equality. Armin Falk and Johannes Hermle in *Science*, Vol. 362, Article eaas9899; October 19, 2018.

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WOMEN'S WORK

As more women contribute to the economy, life gets better for everyone. Why are the barriers to opportunity so hard to change?

By Ana L. Revenga and Ana Maria Munoz Boudet

OVER THE PAST 50 YEARS women and girls in developing countries have made enormous progress. Plenty of data illuminates this trend. Take life expectancy at birth: it went from 54 years in 1960 to 72 years in 2008. During the same period, we experienced the world's fastest ever decline in fertility. These changes reflect gains for women on many fronts, including education, employment, access to reproductive health and decision-making power, and it all happened much faster than it did in today's rich countries. It took India 44 years and Iran just 10 to reduce the number of children born to a woman from six to three; in the U.S., it took 123 years. Two thirds of all countries have reached gender

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CLOSING THE GENDER GAP in employment would raise productivity by 12 percent in sub-Saharan Africa.

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parity in primary education enrollment, and in more than a third, more girls than boys are in school. In a striking reversal of historical patterns, women now represent the majority of university graduates. And more than half a billion women joined the labor market in the past three decades, which means that today four in 10 workers globally are women.

Yet amid all this progress, the remaining gaps are stubbornly resistant to closure. Although women on the whole live longer than men, in parts of the world such as sub-Saharan Africa they are as likely to die in childbirth as northern European women were in the 19th century before the introduction of antibiotics. Women still hold fewer positions of power in politics and business. And although many women work for pay, they do so under circumstances that weigh their talent, abilities and education differently from those of men.

These inequities are outrageous, and addressing them is both a rights issue and a fundamental objective of development. Just as we think development translates into less poverty and improved access to services for everyone, we also see it as a process of expanding freedoms. It promotes the ability to seize opportunities and decide on a life path. For us, pursuing gender equality—especially in women's access to income-generation opportunities—is a smart policy that itself leads to better development, not just the other way around.

Fully closing the well-being gap between the sexes requires specific, timely and intentional action. There are a few primary ways of doing this. First, remove the barriers that prevent women from having the same access as men to economic opportunities; this can generate higher productivity, and hence higher incomes, for all people. Second, increase women's education, health and overall agency, which results in better outcomes for both mothers and their children. Third, put more women in positions of power. Giving women a representative voice shifts policies and spending toward issues such as sanitation, schooling and health. If only implementing these changes were as easy as identifying them.

IN BRIEF

Improving women's access to economic opportunity, education and reproductive freedom leads to better well-being for all. **Despite significant global progress** in closing gender gaps, especially in developing countries, the remaining disparities between women and men are resistant to change. **Policies and programs** that address entrenched social norms are the most promising solutions and must be intensified and expanded.

A PERSISTENT GAP

UNEQUAL ACCESS to economic opportunity is one of the major hurdles preventing progress. This is a problem in all countries, rich and poor, and in all industries, from farming to entrepreneurship.

The first roadblock is simply a barrier to entry: women must be able to access the economic space to participate in it. Although the female labor force has grown considerably in most parts of the world, a substantial participation gap is visible everywhere between men and women—53 percentage points in the Middle East and North Africa. Even if women can manage to break through that barrier, they are probably not competing on a level playing field. Female farmers have a more difficult time obtaining fertilizers, machinery and improved seed varieties, so their yields are often lower. Likewise, female entrepreneurs often have restricted access to capital and credit. Sometimes that is because they are less likely to own land or other assets required as collateral; other times it is because application procedures require a male co-signer or because banks assign female applicants a higher risk rating than male ones. This means that women-owned businesses are often less profitable, creating a chicken-and-egg cycle that is difficult to break. When these issues are corrected, overall productivity dramatically increases. A recent study showed that closing the gender gap in entrepreneurship would raise productivity and incomes by 12 percent in sub-Saharan Africa and 38 percent in the Middle East and North Africa.

Even in places such as the U.S. and Canada, where the labor-participation gap between sexes may fall below 15 percentage points, other factors hinder equality. Men and women tend to concentrate in different economic sectors, and it is easy to observe that women are more likely to work in education and social services,

HEAVILY "FEMINIZED" SECTORS, such as food production and teaching, tend to have lower wages. In all sectors, men still make more than women who hold the same position, even after factoring in education and age.

EDWIN REMSBERG *Getty Images (coffee plantation in Costa Rica);* A. MAJEED *Getty Images (girls' school in Pakistan)*

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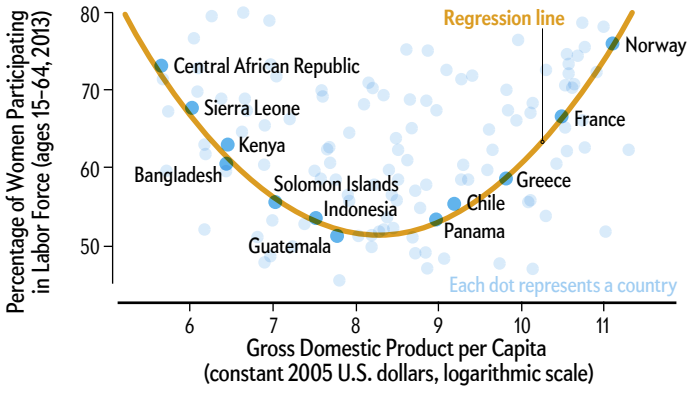
A Labor U-Turn

Female labor force participation tends to be high during the early stages of economic development, when countries are poor and households cannot afford for anyone not to work. A large part of the work is agricultural production. As countries transform from rural societies into industrial or urbanized ones and more income starts flowing into homes, the types of jobs change, and more women stop working. As countries mature into modern service economies, women return to work but in different economic spaces.



SOURCE: ANA MARIA MUNOZ BOUDET (*data from World Development Indicators, World Bank*)

whereas men are more likely to work in construction and transport. But what is less noticeable is that women often occupy the lower-paid roles in whatever sector they are in. For instance, women are often teachers, nurses and clerical workers instead of principals, doctors and supervisors. Even as entrepreneurs, they tend to concentrate in traditionally female sectors such as food or clothing production.

Although we could discuss the preferences women (and men) might have for certain sectors, these patterns are not random. The problem is that those "preferences" reflect the influence of ideas and norms about "women's work" and "men's work" as well as other gendered attributes, such as the notion that women are better caregivers, whereas men are better suited for heavy physical work. The critical point is that heavily "feminized" sectors tend to have, on average, lower wages. And, of course, the gender difference in earnings is well known: Globally, a woman earns about 81 cents for each dollar a male worker earns. In Jordan and Côte D'Ivoire, the difference between incomes is more than 80 percent. Rich countries are not exempt: New Zealand has a low of about 5 percent; it is 36 percent in South Korea. But this difference reflects the different economic positions women hold. Even when you factor in characteristics such as education, sector and age that will make a female and male worker otherwise equal, the income gap persists. Female teachers in rural Pakistan, for instance, earn about 30 percent less than male teachers. Understanding—and addressing—the entrenched social norms behind these persistent gaps is key to closing them.

STUBBORN SOCIAL NORMS

ONE OF THE MAJOR CAUSES of lower earnings and productivity stems from constraints on women's time. Women devote far more of their days to care and household work than men, which in turn means that women have less time for paid work. Deep-rooted social norms drive the differences in "domestic" roles. What is most striking is that these norms, and hence patterns of time use, do not change even as women take up a larger share of market work. In Ghana, a wife still does more than 80 percent of the housework even when she brings home all the income. This imbalance is largely true elsewhere as well, including the U.S. Even in the most progressive places, this pattern reflects assumptions about the division of roles, identifying them as natural and biological instead of cultural. As such, we all live as though this is just the way things are. You can see the effects everywhere in the workings of societies, households and markets. Look at school schedules, which are not consistent with a full-time employment day, or laws that allow mothers—but not fathers—to use sick days to care for an ill child. Breaking these patterns requires upending default expectations.

Unfortunately, policies used to address the time-constraint issue primarily work around these norms instead of confronting them head on. While the results are promising, it's not a complete solution. The most popular example of this is providing increased access to child care services and improving parental-leave policies. As expected, the expansion of access to early child care and preschool services consistently leads to higher labor-market participation of women across all countries. Expanding child care accessibility (location, times of operation), affordability (direct and related costs) and capacity (removing waiting lists, including different ages of children) has a positive impact on the mother's labor engagement.

There is ample evidence that this policy change often alleviates constraints on working mothers' time. In the early 1990s Argentina embarked on a program to expand early childhood education. It resulted in the creation of 175,000 preschools over seven years. Researchers observed labor patterns as the program expanded and found a positive impact of between 7 and 14 percentage points in mothers' employment. Most notably, these positive effects hold even when the preschool is only part-time.

But policies such as allocating more time to maternity leave—and adding paternity or parental leave to include fathers—have not always been as successful. In Germany, the expansion of maternity-leave regulation and coverage led more women to ultimately return to work with their prebirth employer. But when neighboring Austria shifted its maternity leave duration in 1990 from one year to two years, it significantly reduced the percentage of women who returned to work at all.

Then there are the parental-leave programs in Scandinavian countries, which give fathers an incentive to share the load after the birth of a child. When they were

Graphic by Jen Christiansen

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first introduced, they were rarely used by men. But when such a policy in Sweden specifically gave fathers dedicated, nontransferable leave, it delivered positive results in terms of getting fathers to spend more time with their children. Studies have shown that these men remain very involved in parenting over time but slowly transition out of other domestic tasks as the leave effect ends.

Similarly, differences in human capital often affect women's career trajectories. The root of the problem is not a difference in ability or capacity between the sexes—it is discrepancies in how we invest in and value women as workers. In developing countries, these differences appear as access to and completion of education; in more developed countries, where educational attainment is higher and both men and women attend university in large numbers, gender differences show up in fields of study. In the U.S., for example, women represent less than 35 percent of the degrees in the science and technical fields even though they account for almost 60 percent of college graduates.

When it comes to bridging human capital between men and women, governments must make investments beyond traditional education to include training, apprenticeships and other labor policies. Young job seekers are an important target of these policies. One notable example is the series of Jóvenes (youth) programs implemented across Latin America in the early 2000s, which encompassed a combination of training, internships and incentives to employers with a goal of breaking biases in hiring young workers. Across the board, these programs increased the probability of young women becoming employed and boosted their earnings.

But efforts to translate the lessons from the Jóvenes programs to other settings have had uneven results. An evaluation of a similar vocational-training program in Malawi found that family obligations limited female participation. The Jordan New Opportunities for Women pilot involved more than 1,000 young women from community colleges. Demand for the program was extremely high: many of these women successfully completed the vocational training, and half of those graduates found jobs thanks to wage-subsidy vouchers provided for employers. But the effects were short-lived, and no changes were found in employment or earnings. Here again, it appears that social norms and employers' views about women heavily impeded successful replication of the initiative.

The third driver of gender inequality in economic opportunities is what we would typically call discrimination: the differential treatment of women by markets and institutions. When few women are employed in a certain sector, employers may hold biased beliefs about their qualifications. They may be reluctant to hire women because they associate extra costs, such as maternity leave, with female employees, or they may assume that women are not the primary breadwinners and therefore lack motivation. A number of studies that compare the reactions of employers with otherwise identical female and male CVs found substantial evidence of gender discrimination when it comes to recruitment and hiring. Moreover, access to jobs often involves gendered networks: when women are poorly represented in an occupation, they are less likely to become aware of opportunities and may be unable to find mentors. In many countries, gender-specific job advertisements and gender-biased selection criteria and recruitment are still common. In an astonishing 174 of the 189 countries in the Women, Business and the Law database, employers are not prohibited from asking job applicants about family status and family planning.

Government institutions can also treat men and women differently, often in ways that play against women's interests. For example, in 66 percent of countries, women cannot do the same jobs as men. Many former Soviet countries are particularly restrictive. In Russia, there are nearly 460 occupations currently forbidden to women, including steelworker, firefighter, oil-well worker and bus operator. Others countries require women to get male permission to accept jobs, open bank accounts or operate businesses. In Chile, husbands have the sole right to administer marital property, regardless of whose income or savings was used to purchase the property. In Pakistan, a married woman cannot register a business in the same way as a married man. In Mongolia, many women cannot work at night. In

THOMAS TRUTSCHEL Getty Images (farm in Bangladesh)

WOMEN perform the lion's share of household duties, even in the most progressive countries.

IN GHANA, A WIFE DOES MORE THAN 80 PERCENT OF THE HOUSEWORK EVEN WHEN SHE BRINGS HOME ALL THE INCOME. SUCH IMBALANCES ALSO EXIST IN THE U.S.

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Yemen, a husband can object to a wife's employment.

These three sets of differences between men and women—in responsibilities for care and housework, in human capital investments, and in treatment by markets and institutions—not only get in the way of equitable economic opportunities but often do so in ways that reinforce one another. Devoting much more time to care and housework may encourage women to self-select occupations that offer greater flexibility in hours but trap them into lower pay. This is especially true if formal employment options come with restrictions on part-time work, as is the case in many developing countries. Preemptively knowing it will be hard to get a job—and fit in—in a male-dominated field such as engineering or construction may discourage girls and young women from acquiring the education and skills necessary to pursue those opportunities. And repeated experiences of discrimination in job applications and hiring may push women toward informal self-employment or discourage participation in the labor market altogether, which starts the cycle of inequality all over again.

FINE-TUNING THE SOLUTIONS

WHY, IF WE HAVE been able to clearly identify the roots of the gender gaps in economic empowerment, does change remain so elusive? For starters, the multiplicity of factors requires many actions coordinated toward the same goal. And given that the nature, structure and functioning of markets, institutions and norms vary widely across countries, a one-size-fits-all policy approach is impossible. As we have shown, policies that were successful in one context may face significant resistance in another.

Still, a few general principles have proved critical for successful policies. To be effective, policies and interventions need to target the multiple underlying factors that drive gender differences in access to economic opportunities. That is, they need to directly address the constraints on women's time that arise from gendered social norms about care and housework, not circumnavigate them. To increase productivity, they must fill the gaps in information, skills and access to professional networks that constrain the opportunities of female wage workers, farmers and entrepreneurs. And they need to help build a more level playing field in markets and institutions by targeting discriminatory preferences.

One such promising example of a dynamic intervention hits many of those targets. The Empowerment and Livelihood for Adolescents program (ELA) implemented in Uganda by the nongovernmental organization Building Resources Across Communities provided young women aged 14 through 20 with life skills and vocational training at "girls' clubs" where a mentor was present to lead activities. The clubs also served as a safe space in which adolescent girls could meet, socialize and recreate. A quarter of the girls in the 100 communities selected for the evaluation participated in the program, and the results were impressive. Girls in ELA communities were 72 percent more likely to be engaged in an income-generating activity four years later. But most important, the program shifted the girls' attitudes and aspirations. For example, the participants were more likely to believe that women should earn money for their families and less likely to be worried about finding a good job in adulthood. Strikingly, those shifts helped teen pregnancy rates fall by 34 percent, and early entry into marriage or cohabitation dropped by 62 percent.

Policy makers, too, must learn from their own successes and failures and those of others. To achieve that, they must be able to clearly articulate both what goes into the policy and its expected impact. These initiatives also need to be piloted and properly evaluated before taken to scale. Too many interventions designed to support gender equality rely only on good intentions and intuitions. While some might deliver in terms of outputs—say, the number of women who received training from a vocational program—many fail to deliver the expected final outcome, which in this case means getting more women to enter (and stay in) the labor market.

Policies and programs that show the greatest potential should be expanded and intensified. They must not be stopped even once the desired objective seems to be achieved—long-term follow-through is especially critical when tracking social changes as well as logistical ones. Progress requires constant, concerted and coordinated action to make markets, institutions and societies as a whole work more fairly for women, and changing the long-standing norms about women's and men's roles both at home and at work is a tall order. Resources for gender-specific interventions compete with other urgent development priorities, such as food security and poverty reduction. And goals like those can have no specific effects on closing gender gaps. That is why it is essential to rely on tested and proven tactics instead of leaning too heavily on advocacy and good intentions.

Greater gender equality is achievable with a combination of political will and evidence-based policies. Women and men of the future all stand to benefit from a more equitable society. SA

UNEQUAL SEATING

Only around **20** women hold the office of head of state or government around the world.

A mere **23%** of parliamentary seats are occupied by women globally.

Rwanda has the highest female representation: **61%** of the 80 seats in the country's lower house are held by women.

SOURCES: FACTS AND FIGURES: LEADERSHIP AND POLITICAL PARTICIPATION, U.N. WOMEN *www.unwomen.org/en/what-we-do/leadership-and-political-participation/facts-and-figures* (heads of state or government); WOMEN IN NATIONAL PARLIAMENTS: SITUATION AS OF JUNE 1, 2017. INTER-PARLIAMENTARY UNION *www.ipu.org/wmn-e/world.htm* (parliamentary seats)

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Ana Maria Munoz Boudet is a senior social scientist at the Poverty and Equity Global Practice at the World Bank Group. She is part of the bank's Mind, Behavior, and Development Unit.

MORE TO EXPLORE

World Development Report 2012: Gender Equality and Development. World Bank, 2012.
Aggregate Effects of Gender Gaps in the Labor Market: A Quantitative Estimate. David Cuberes and Marc Teignier in *Journal of Human Capital*, Vol. 10, No. 1, pages 1–32; Spring 2016.
Breaking the STEM Ceiling for Girls. Ana Maria Munoz-Boudet and Ana Revenga in Future Development blog, Brookings Institution. Published online March 7, 2017.

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MIND THE GAP

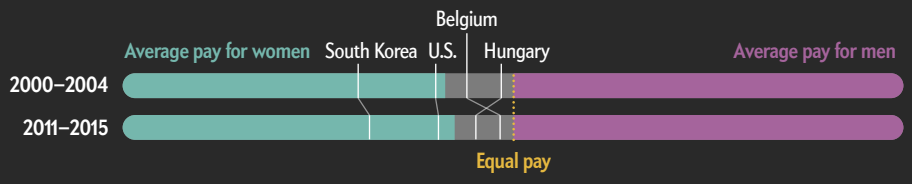
Gender inequality remains a global phenomenon

By Amanda Montañez

Data from the past few decades show that despite progress toward gender equality, many challenges persist. Women are still disadvantaged compared with men where access to economic and social opportunities is concerned. Some of these so-called gender gaps, such as the dearth of women in government, stem from societal attitudes about gender and leadership. Others arise from factors that by definition disproportionately affect women, such as restrictions on reproductive health care. (Reporting on this story relied on data available in 2017.)

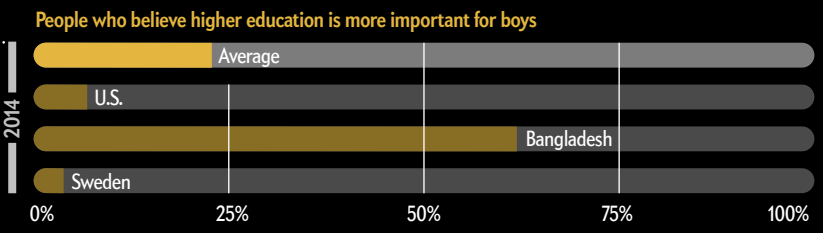
PAY

Across the globe, female employees earn less on average than their male counterparts. Despite improvement over the past decade, none of the 31 countries represented here has eliminated the gender wage gap.



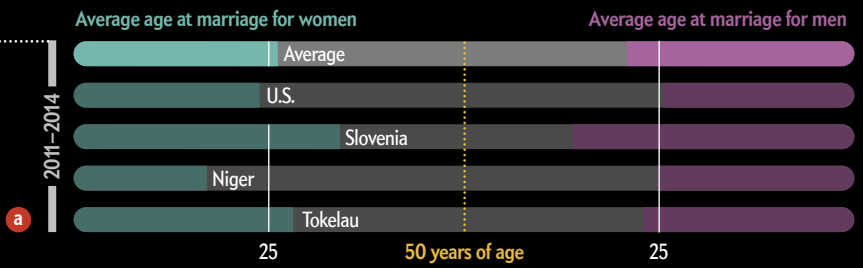
EDUCATION

In some parts of the world, including the U.S., women make up more than 50 percent of college graduates. But globally, nearly a quarter of the population thinks that university education is more important for boys than girls. This chart includes data from 85 countries.



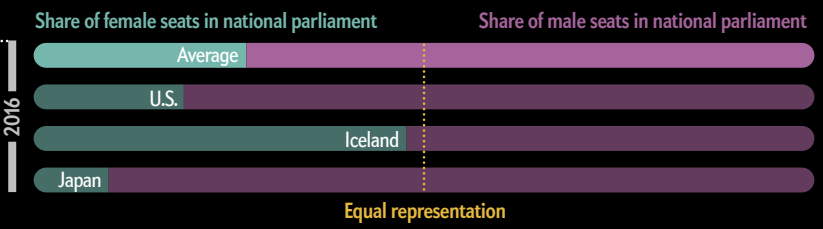
MARRIAGE AGE

Women tend to get married at younger ages than men. Based on data from 104 countries and territories, this chart represents the average age of those who marry before age 50.



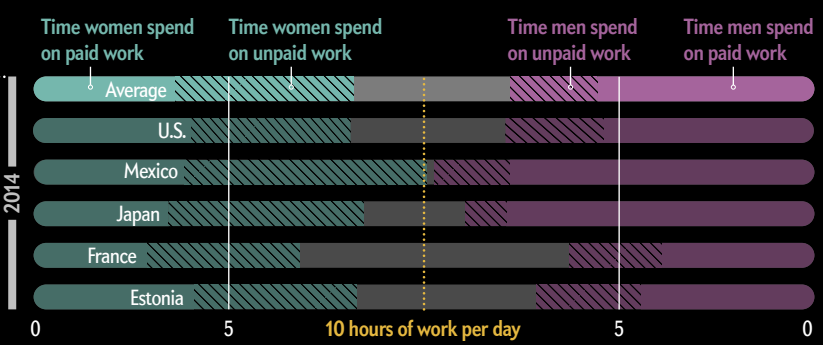
SEATS IN GOVERNMENT

Although they make up roughly 50 percent of the population, women are vastly underrepresented in government. Drawing data from 44 countries, this chart shows the average share of female seats in national parliaments.



UNPAID WORK

Women spend more time working every day than men do, but a comparatively high percentage of that labor is unpaid. Tasks such as child care and housework contribute to the imbalance represented in this chart, which draws on data from 29 countries.



GENDER GAPS

Graphic by Amanda Montañez

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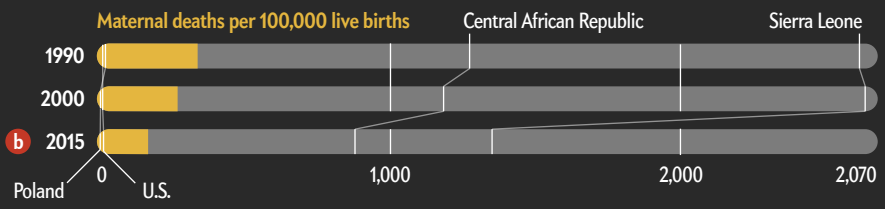
RECENT PROGRESS

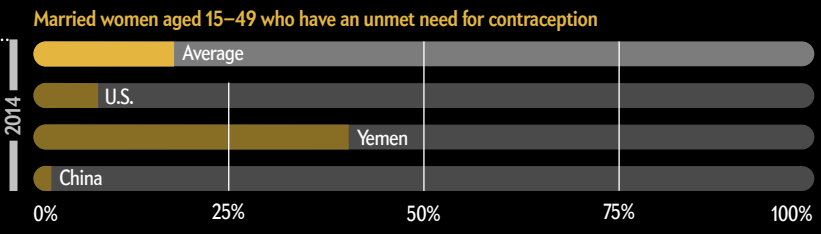
MATERNAL MORTALITY

Data from 181 countries and territories show that, on the whole, the rate at which women die of causes related to pregnancy or childbirth has been steadily declining over recent decades. That rate remains high in many developing countries, however.



CONTRACEPTION

Data from 120 countries indicate that, globally, about 18 percent of married women between the ages of 15 and 49 have an unmet need for contraception.

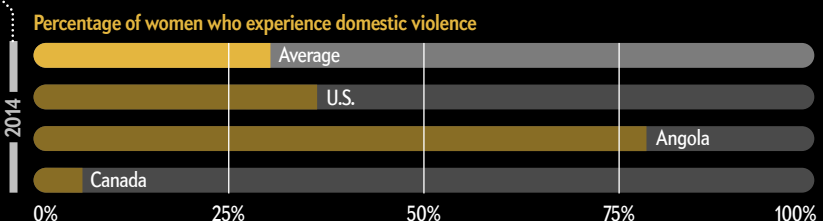


PAID PARENTAL LEAVE

Women shoulder most of the responsibility of child care, particularly during infancy. Most national governments mandate some amount of paid time off work for new parents, according to data from 160 countries. In those outlying countries that fall short in this category—including the U.S.—mothers disproportionately pay the price.

DOMESTIC VIOLENCE

Data from 103 countries reveal that a high percentage of women suffer physical or sexual violence from an intimate partner at some point in their lives.



ACCESS TO ABORTION

Abortion remains illegal or restricted in most of the 160 countries represented here. Constraints on abortion access range from gestational limits (such as banning abortion after 20 weeks) to laws that allow abortion only in cases of rape or incest or when the life of the mother is endangered.

ISSUES PRIMARILY AFFECTING WOMEN

a The small New Zealand territory of Tokelau is one of the few places in the world where brides are slightly older on average than grooms. The mean age at marriage there is around 28 for women and 27 for men.

b The maternal mortality rate in the U.S. is well below the global average. It is higher than that of other wealthy countries, however, and has increased in recent years, from 12 deaths per 100,000 live births in 2000 to 14 per 100,000 in 2015.

c Clinicians generally recommend that mothers who have given birth exclusively breastfeed their infants for the first six months of life, making that interval a logical minimum for paid maternity leave.

SOURCES: RESEARCH BY AMANDA HOBBS; UNITED NATIONS DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS (*marriage data*); WORLD HEALTH ORGANIZATION (*maternal mortality data*); WORLD BANK (*parental leave data*); ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (*pay gap, education, paid/unpaid work, contraception, domestic violence* and *abortion data*)

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MEN WHO ADVOCATE FOR OTHERS IN THE WORKPLACE FACE BACKLASH

Study shows a cost for males who defy gender stereotypes

By Daisy Grewal

GETTY IMAGES

Back in March 2018 a group of Hollywood elites signed an open letter asking men to take more responsibility for creating workplaces that are free of sexism. The letter was in response to the #MeToo movement that spurred people across the world to use social media to bring attention to the prevalence of sexual harassment and abuse. The letter signers pledged to act as advocates for victims and to speak out openly against sexism, thereby launching #AskMoreofHim, a movement that highlights the role that men play in preventing gender-based violence.

It seems reasonable to assume that men, especially those occupying positions of power, are in a unique position to act as advocates and allies for victims of sexism and sexual violence. Recent research, however, indicates that men may face a backlash for speaking out on behalf of others. Janine Bosak of Dublin City University in Ireland and her colleagues published a study suggesting that men who take on an advocacy role in the workplace may suffer penalties for going against how we typically expect men to behave. Although the study did not look at men who speak out against sexual bias per se, it strongly implies that men who advocate for others in general may be seen as less competent.

Common stereotypes about men hold that they show ambition at work and focus most of their energy on promoting themselves and their own accomplishments. In contrast, stereotypes about women involve emphasizing other people's feelings and welfare above their own. Social scientists have shown that people who act contrary to these stereotypes tend to elicit "backlash" from both men and women. This backlash may take the form of being seen as less likable, less competent and less suitable for certain jobs.

The researchers recruited 149 working professionals to participate in an online study that was ostensibly about "perceptions and decision-making." The participants were evenly divided by gender, and although they held a variety of jobs, the majority worked in human resources. Each participant was presented with written application materials from either a man or woman job candidate.

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The candidate was described as someone who tends to advocate either primarily for himself or herself or for the team. For example, the self-advocating applicant was described as "a fierce worker who diligently works for success" and "wants to receive credit where due and is excellent at promoting himself." In contrast, the other-advocating applicant was described as "a strong negotiator on behalf of this team" and "a fierce worker who diligently guides his team to success." After reviewing the application materials, participants filled out a survey asking them about their impressions of the candidate. Specifically, they rated the candidate's likability, competence and how much they would recommend that the person be let go if the company were to downsize. Overall, the findings supported the idea that men who advocated for others were seen less positively. Both men and women rated the other-advocating man as less competent, and they were more likely to recommend that he be laid off in the event of downsizing. Participants also liked the other-advocating man less than they liked the other-advocating woman.

Surprisingly, study participants did not display the same kind of backlash toward the woman applicant who was described as being highly self-advocating. Previous research has demonstrated that people penalize women who behave in highly self-promoting ways; however, this study did not find that to be true. The researchers offer two possibilities for this unexpected finding: earlier studies had participants watch videos of job candidates, which may elicit stronger reactions than just reading written materials, and many of the study participants were trained human resource professionals who may have been more attuned to biases against women.

Backlash against atypical men poses a serious dilemma for those who believe that men are vital to helping battle workplace inequality. We know that men, and in particular white men, are more likely to hold leadership positions in a variety of industries. Movements such as #AskMoreofHim rest on the assumption that men will be motivated to advocate for others if they are sufficiently convinced to do so. The present research, however, suggests that men may shy away from advocacy to avoid being perceived negatively by others. Although we may laud the integrity or compassion of men who speak out on others' behalf, we may simultaneously question their competence compared with men who do not advocate for others. Therefore, when it comes to fighting sexism and gender-based violence, we might want to start by examining how our own stereotypes may be contributing to the problem. By loosening up our expectations for people of all genders, we can help ensure that individuals feel free to act in ways that promote equality for all in the workplace. SA

Daisy Grewal holds a B.A. in psychology from the University of California, Los Angeles, and a Ph.D. in social psychology from Yale University. She is a senior research scientist for people analytics at Intuit in Mountain View, Calif.

MORE TO EXPLORE

Reactions to Counterstereotypic Behavior: The Role of Backlash in Cultural Stereotype Maintenance. Laurie A. Rudman and Kimberly Fairchild in *Journal of Personality and Social Psychology,* Vol. 87, No. 2, pages 157–176; August 2004.

Be an Advocate for Others, Unless You Are a Man: Backlash against Gender-Atypical Male Job Candidates. Janine Bosak et al. in *Psychology of Men and Masculinity,* Vol. 19, No. 1, pages 156–165; January 2018.

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The Brilliance Trap

How a misplaced emphasis on genius subtly discourages women and African-Americans from certain academic fields

By Andrei Cimpian and Sarah-Jane Leslie

IN BRIEF

Academic fields that prize the brilliance of their members, the authors found, are likely to be less diverse in gender and racial makeup.
Although innate cognitive ability is not, as far as scientists can tell, tied to gender or race, it is psychologically easier to ascribe this trait to people from groups stereotypically assumed to be intelligent.
Women and African-Americans may subconsciously interpret a field's emphasis on brilliance as a subtle "Keep Out" sign that dissuades them from entering certain disciplines in the sciences and humanities.

Illustrations by Allison Seiffer

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IN THE 1980S PHILOSOPHERS would sometimes speak of "the Beam"—a metaphorical spotlight of intellectual brilliance that could illuminate even the most complex philosophical conundrums. Only some lucky philosophers were ever born with the Beam, and their work represented the gold standard of the field. Anyone who lacked the Beam was forever condemned to trail behind them intellectually.

One of us (Leslie) would share this sort of story whenever we would see each other at conferences. The two of us were trained in different disciplines (Leslie in philosophy and Cimpian in psychology), but we studied similar topics, so we would get together regularly to catch up on research and talk about our experiences as members of our respective fields. Psychology and philosophy are quite similar in their substance (in fact, psychology was a branch of philosophy until the mid-1800s), but the stories we told painted a picture of two fields with vastly different views on what is important for success. Much more so than psychologists, philosophers value a certain kind of person—the brilliant superstar with an exceptional mind. Psychologists, in contrast, are relatively more likely to believe that the leading lights in their field grew to achieve their positions through hard work and experience.

At first, we viewed philosophy's obsession with brilliance as a quirk—a little strange but innocuous. Other things seemed like bigger problems in Leslie's field, such as its inability to attract women and minorities. Despite sustained attention to issues of underrepresentation in recent years and some efforts to alleviate them, women still accounted for fewer than 30 percent of the doctoral degrees granted in philosophy in 2015; African-Americans made up only 1 percent of philosophy Ph.D.s. The field of psychology, on the other hand, has been quite successful in attracting and retaining women (72 percent of newly minted Ph.D.s), and African-Americans held 6 percent of its 2015 doctoral degrees, which admittedly still falls short of their share of the general population but is nonetheless six times the ratio in philosophy.

We could not wrap our minds around the discrepancy. Our fields have so much in common—both philosophers and psychologists ask questions about how people perceive and understand the world, how they decide between right and wrong, how they learn and use language, and so on. Even the few salient differences—such as psychologists' greater use of statistics and randomized experiments—are becoming blurred nowadays with the huge increase in the popularity of experimental philosophy, in which philosophers conduct surveys and experiments to explore different perspectives on morality, for example. How could two such closely related fields be so vastly different in membership?

A BRILLIANT IDEA

THE CLOSEST THING either of us has ever had to a eureka moment came several years ago when we connected two threads running through the anecdotes we had been sharing. We were having dinner with a group of philosophers and psychologists at a conference, and the conversation happened to turn, in quick succession, from philosophers' infatuation with brilliance to the gender gap in their field. This chance juxtaposition brought to mind for us a connection we had never considered before: maybe the premium that philosophers place on brilliance is actually the reason so few of their colleagues are women or minorities. We did not discount the benefits of brilliance. Rather we wondered whether genius was more easily overlooked in women and African-Americans. Could it be that insistence on the need for a keen intellect in a particular field was tantamount to hanging a "Keep Out" sign to discourage any newcomers who did not resemble that field's current members?

On the surface, an emphasis on brilliance does not favor one group over another; as far as scientists can tell, cognitive ability is not intrinsically tied to gender or race. Philosophers seek a certain quality of mind—regardless of whose mind it is. This seemingly logical preference quickly becomes problematic, however, in light of certain shared societal notions that incorrectly associate superior intellect with some groups—for example, white males—more than others.

Even among the academics present that night, one of the views expressed was that men and women just thought differently. Women were alleged to be more practical and anchored in reality, whereas men were more willing to engage in the kind of counterfactual, abstract reasoning that is viewed as a sign of philosophical brilliance. We started to wonder whether such stereotypes, which amount to equating brilliance with men, might well dissuade women from entering a field that holds this quality in high esteem. Moreover, current members of such a field might themselves hold different expectations about the prospects of men and women and might evaluate and encourage them differently as a result. The same logic extends to race: our country has a long history of portraying African-Americans as intellectually inferior, which is particularly likely to affect their participation in a field that focuses so single-mindedly on the quality of one's intellect. Considering these stereotyped attitudes, which are unsupported by science, philosophy's fascination with brilliance may have a real impact on its diversity.

Later that night the two of us talked about our insight. We speculated whether its implications extend beyond our home disciplines. Talk of brilliance is common in academia and—it seemed to us—quite common in fields that have similar issues with diversity, such as science, technology, engineering or mathematics. Might our anecdotal comparison of philosophy and psychology have something new to say about the underrepresentation of women and minorities in these disciplines?

The more we thought about it, the more we realized that our brilliance hypothesis might also explain some of the variability in gender and race gaps *among* different scientific fields. For example, women make up nearly 50 percent of doctoral degrees in biochemistry but just more than 30 percent of Ph.D.s in organic chemistry. The difference cannot easily be explained by the content of the fields, in which there is considerable overlap, or by their history—biochemistry emerged from organic chemis-

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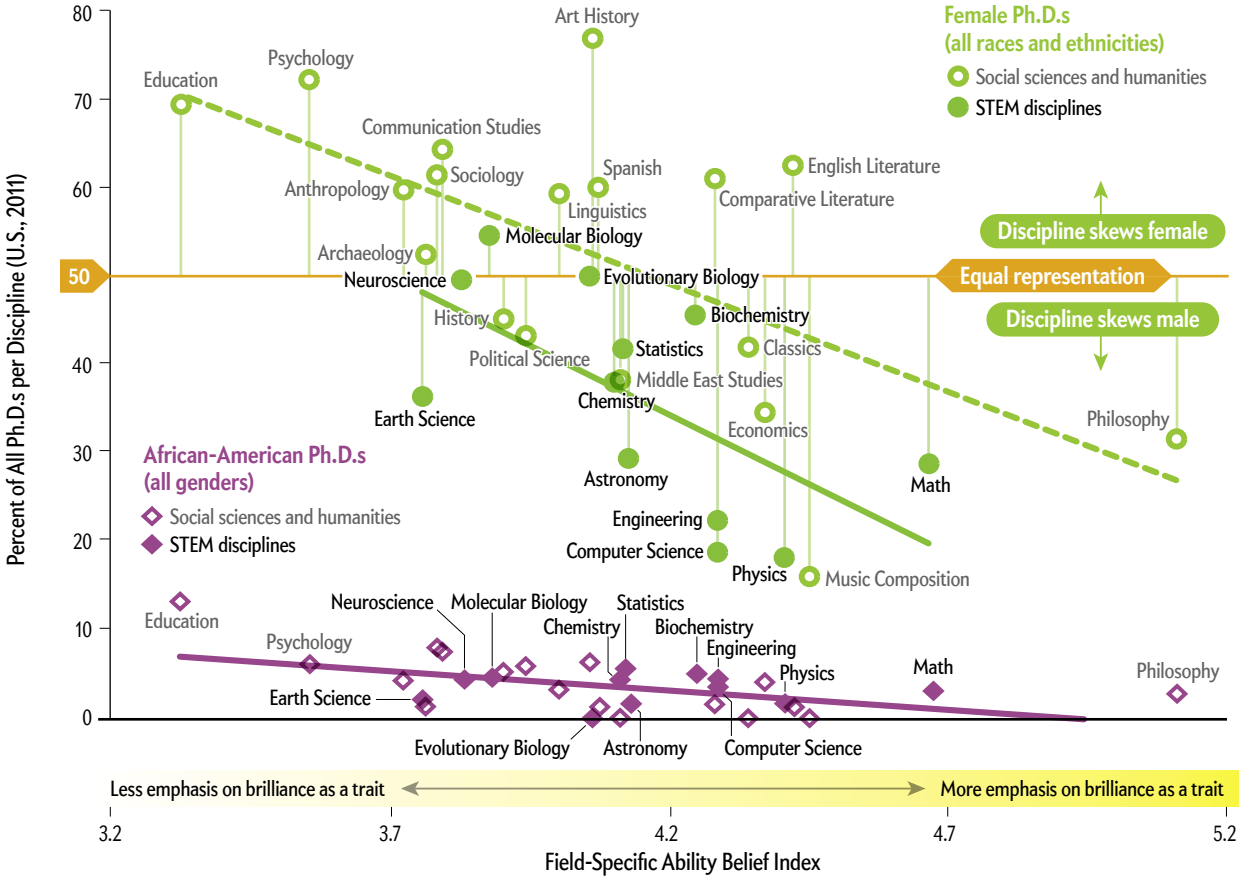
How Stereotypes about Genius Affect Women and Minorities in Academia

A survey of almost 2,000 professionals in 30 academic fields determined how strongly they believed that the trait of brilliance, as measured by a so-called field-specific ability belief index, mattered for success in their discipline. Fields with higher scores, such as physics, math and philosophy, awarded fewer advanced degrees to women and African-Americans, compared with neuroscience and psychology, which scored lower. The results suggest that many fields implicitly equate brilliance with white males.



try at about the same time psychology separated out of philosophy as an independent discipline. We wondered whether the demographic differences between such sibling subjects, as well as more generally among scientific fields, could be explained in part by the extent to which they emphasize exceptional intellectual talent as the key to success.

SUCCESSFUL MINDSETS

OUR EARLY CONJECTURES quickly reminded us of the rich body of work developed by psychologist Carol S. Dweck of Stanford University. Dweck and her colleagues have shown that one's beliefs about ability matter greatly for one's ultimate success. A person who sees talent as a stable trait (a "fixed mindset" in Dweck's terminology) is motivated to show off this aptitude and avoid mistakes, which presumably reflect the limits of that gift. In contrast, a person who adopts a "growth mindset" sees his or her current capacity as a work in progress. In other words, ability is a malleable quantity that can usually be increased with more effort and better strategies. For a person with a growth mindset, mistakes are not an indictment but rather a valuable signal highlighting which of their skills are in need of work.

Although Dweck initially studied mindsets in individuals, she and Mary Murphy, now at Indiana University Bloomington, recently suggested that organized groups of people, such as companies and clubs, may also hold these sorts of views. We took that idea a step further and considered whether they might permeate entire disciplines as well. The fascination with brilliance in philosophy and other areas could conceivably create an atmosphere in which displays of intellectual prowess are rewarded, and imperfections are to be avoided at all costs. In combination with the stereotypes suggesting that genius is unevenly distributed across groups, such a field-wide perspective could easily turn tox-

SOURCE: "EXPECTATIONS OF BRILLIANCE UNDERLIE GENDER DISTRIBUTIONS ACROSS ACADEMIC DISCIPLINES," BY SARAH-JANE LESLIE ET AL., IN *SCIENCE*, VOL. 347; JANUARY 16, 2015

Graphic by Jen Christiansen

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ic for members of stereotyped groups, such as women or African-Americans. After all, it is easy to "see" imperfections and inadequacies in those people whom you expect to have them.

Several long phone conversations later, we had a tentative plan for putting our ideas to the test. We would contact academic professionals from across a wide range of disciplines and ask them whether they thought that some form of exceptional intellectual talent was necessary for success in their field. We would then look up statistics on the gender and racial/ethnic composition of the people obtaining Ph.D.s in these disciplines, which the National Science Foundation freely supplies on its Web site. If our hunch was correct, we should see that those disciplines that place more value on brilliance would tend to have fewer female and African-American Ph.D.s. This pattern should hold not just at the macro level—when comparing the hard sciences, for example, with the social sciences and the humanities—but also *within* these broad domains—for disciplines as similar as philosophy and psychology.

More than a year and thousands of e-mailed surveys later, we and our collaborators Meredith Meyer of Otterbein University in Ohio and Edward Freeland of Princeton University finally had an answer to some of our questions. Equal parts relieved and exhilarated, we saw that the answers received from almost 2,000 academics across 30 fields matched the distribution of Ph.D.s in the way we had expected. Fields that placed more value on brilliance also conferred fewer Ph.D.s on women and African-Americans. The greater the emphasis on this single fixed trait, the fewer doctoral degrees were awarded to either of these groups. The proportion of female and African-American Ph.D.s in psychology, for example, was higher than the parallel proportions for philosophy, math or physics.

Next, we separated the responses in the physical and biological sciences from those in the humanities and social sciences. Analyses of these subgroups indicated that a stronger emphasis on brilliance correlated with fewer female and African-American Ph.D.s regardless of whether we compared physics with biology or philosophy with sociology. It seemed that we had stumbled onto an explanation that was general enough to describe the representation of multiple stereotyped groups in fields across the entire academic spectrum.

ALTERNATIVE IDEAS

OUR EXCITEMENT ABOUT THESE DATA ASIDE, all we had really shown at this point was a correlation between the presumed desirability of a fixed trait—brilliance—with a dearth of women or African-Americans in a given field. We had not yet demonstrated cause and effect. Certainly many other plausible explanations for the gender imbalances have been proffered over the years—from a heavier workload that favored single men and those with wives who did not work outside the home to a supposed female preference for working with living organisms, as opposed to inanimate objects. We needed to determine whether we were bringing something new to the table—perhaps our explanation reduced to one that had been previously offered.

We carefully examined the most common alternatives. For instance, did our brilliance measure simply track differences between fields in their reliance on math? We looked at the math portion of incoming students' Graduate Record Examinations (GREs) as a proxy. Beliefs about brilliance still predicted women's representation above and beyond those scores. Similarly, we found no support for the common view that women are underrepresented in "high-powered fields" because they prefer a better work-family balance. We asked the academics in our sample how many hours they worked per week—both on- and off-campus. Taking into account these differences in workload did not, however, reduce the explanatory power of beliefs about brilliance; this single variable still predicted the magnitude of gender gaps across the 30 disciplines. We also considered the prevalent thought that women might be more interested in working with (and have a better intuitive understanding of) people, whereas men prefer inanimate systems. But an analysis of the many branches of philosophy, for example, that do in fact consider people—and are still dominated by men—basically blew that idea out of contention.

As often happens in research, this initial study made it clear to us how much we did *not* yet know about the phenomenon that we were investigating. For example, we realized it would

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be important to know if academics' beliefs about brilliance predict gender and race gaps at earlier points in students' educational trajectories. We were very interested in testing our idea at the bachelor's level, which is the gateway to students' later careers. Do field-level messages about the importance of brilliance relate to the majors that young women and African-Americans ultimately pursue?

The answer to this question is yes, as we reported in *PLOS ONE* in 2016 when we analyzed anonymous student evaluations of their college instructors on RateMyProfessors.com. We found that undergraduates were nearly twice as likely to describe male professors as "brilliant" or a "genius" compared with female professors. In contrast, they used such terms as "excellent" or "amazing" equally often for men and women on the popular Web site. We determined that the overall amount of talk about brilliance and genius in the student reviews (which is a proxy for a field's emphasis on these qualities) correlated closely with a lack of diversity in completed majors.

ORIGINS OF STEREOTYPES

FURTHER INVESTIGATION showed that nonacademics share similar notions of which fields require brilliance. Exposure to these ideas at home or school could discourage young members of stereotyped groups from pursuing certain careers (such as those in science or engineering) before they even set foot on a college campus.

At this point, we realized we needed to investigate the acquisition of these stereotypes. When do young people in our culture start thinking that some groups have more brilliant people in them? On the one hand, it could be that this stereotype emerges late in development, after sustained exposure to relevant cultural input (for example, media portrayals of brilliance and gender-biased expectations from parents, teachers, professors and peers). On the other hand, evidence from developmental psychology suggests that children are cultural sponges—incredibly sensitive to signals in their social environments. In fact, youngsters in the early elementary grades seem to have already absorbed the stereotypes that associate math with boys and reading with girls. From this perspective, we might expect that stereotypes about brilliance would also be acquired early in life.

To explore this idea, we asked hundreds of five-, six- and seven-year-old boys and girls many questions that measured whether they associated being "really, really smart" (our child-friendly translation of "brilliant") with their gender. The results, which we published in 2017 in *Science,* were consistent with the literature on the early acquisition of gender stereotypes yet were still shocking to us. Male and female five-year-olds showed no difference in their self-assessment. But by age six, girls were less likely than boys to think that members of their gender are "really, really smart."

Finding these stereotypes so early in childhood made us ask whether they might already begin to constrain boys' and girls' interests. We introduced another group of five-, six- and seven-year-olds to unfamiliar gamelike activities that we described as being "for children who are really, really smart." We then compared boys' and girls' interest in these activities at each age. The results revealed no gender differences at age five but significantly greater interest from boys at six and seven years of age—which is exactly where we saw the stereotypes emerge. In addition, the children's own stereotypes directly predicted their interest in these novel activities. The more a child associated brilliance with the opposite gender, the less interested he or she was in playing our games for "really, really smart children." This evidence suggests an early link between stereotypes about brilliance and children's aspirations. Over the rest of childhood development, this link may funnel many capable girls away from disciplines that our society perceives as being primarily for brilliant people.

The hard work of figuring out how best to put all this information to use—how to intervene—lies ahead of us. But a few suggestions follow pretty directly from the evidence we have so far. Minimizing talk of genius or brilliance with students and protégés may be a relatively easy and effective way of making one's field more welcoming for members of groups that are negatively stereotyped in this respect. Given current societal stereotypes, messages that portray this trait as singularly necessary may needlessly discourage talented members of stereotyped groups. The changes may need to go a little deeper than talk, however, and tackle some of the entrenched, systemic issues that accompany a field's fascination with brilliance. Refraining from mentioning the Beam will not help young women in philosophy if the rest of the field's practices continue to be implicitly anchored in the idea that brilliance is all that matters.

Another key takeaway is that we may need to intervene earlier than conventional wisdom suggests. Our developmental data indicate that some of the psychological processes that work against diversity in fields that value brilliance can be traced all the way back to elementary school. Waiting until college to step in and ensure that all young people have a fair shot at finding the careers that might suit them no longer seems like the best-timed intervention—we as a society would be wise to encourage a growth perspective, as opposed to a fixed-trait mindset, in young children as well. SA

FRIENDLY FIELDS

Of the 17,505 doctorates awarded in science and engineering to women in the U.S. in 2015,

40%

were given in the life sciences.

Of the 1,307 of such doctorates granted to African-Americans, more than

40%

were in psychology and the social sciences.

SOURCE: *DOCTORATE RECIPIENTS FROM U.S. UNIVERSITIES: 2015.* NATIONAL CENTER FOR SCIENCE AND ENGINEERING STATISTICS. NATIONAL SCIENCE FOUNDATION, 2017

Andrei Cimpian is an associate professor of psychology at New York University.

Sarah-Jane Leslie is Class of 1943 Professor of Philosophy at Princeton University.

MORE TO EXPLORE

On Being an "African American Scientist." Raynard S. Kington in *Scientist,* Vol. 27, No. 5; May 2013. www.the-scientist.com/critic-at-large/on-being-an-african-american-scientist-39393

Expectations of Brilliance Underlie Gender Distributions across Academic Disciplines. Sarah-Jane Leslie et al. in *Science*, Vol. 347, pages 262–265; January 16, 2015.

The Frequency of "Brilliant" and "Genius" in Teaching Evaluations Predicts the Representation of Women and African Americans across Fields. Daniel Storage et al. in *PLOS ONE,* Vol. 11, No. 3, Article No. e0150194; March 3, 2016.

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END HARASSMENT

A leader of a major report on sexual misconduct explains how to make science accessible to everyone

By Clara Moskowitz

Sexual harassment is more prevalent in academia than in any sector of society except the military. According to a groundbreaking June 2018 report by the National Academies of Sciences, Engineering, and Medicine, harassment hurts individuals, diminishes the pool of scientific talent and ultimately damages the integrity of science itself. To understand the problem and how best to tackle it, a committee of 21 experts spent two years surveying existing data and commissioning new research. Paula Johnson, president of Wellesley College and co-chair of the committee behind the report, hopes its recommendations will fall on ears ready and willing to heed its advice. *Scientific American* spoke to Johnson about how to move forward. An edited transcript of the conversation follows.

What do we need to do to change the situation?

We found the policies and procedures that are in place are not preventing sexual harassment. We know that you have to go on a path of culture change. We've identified some major areas that have to

THE SUNS IN OUR DAUGHTERS

Unleashing the energy trapped within undereducated girls

By Lisa Einstein

The question on the physics quiz seemed simple enough: "What is the smallest piece of matter that makes up everything in the universe?"

Binta's response: "Binta."

I laughed out loud. You would, too, if you saw tiny Binta, who is one of my smartest seventh graders. Surely she knew the correct answer is "atom." Yet, I mused, a famous equation governing atoms could also apply to her.

$E = mc^2$. The equation says that under the right conditions, mass can become energy, and vice versa. Because light moves so fast, an atom at rest—even with a small mass—contains a great deal of energy. A walnut has enough energy locked in it to power a small city. Mass from the sun radiates as light that warms the earth from 93 million miles away. Tiny masses hide astronomical energy.

Reflecting on Binta's lesson as I walk home through the village, I am almost knocked over by Aissatou's exuberant tackle-hug. A magical six-year-old with a spirit too big to fit her child's body, Aissatou is further evidence of the small but powerful. A year into my Peace Corps service in Guinea, my young neighbor has become my local language teacher, running partner, closest friend and inspiration. I've watched her lead friends through dances she created, make bandages from spare fabric for her injured four-year-old sister and fashion a rope extension so our bucket can reach the bottom of our dried-up well. Aissatou is a designer: she builds, plays and imagines. I observe her ingenuity with awe.

I see Aissatou the way my parents saw me: filled with unlimited potential. My parents called their four kids "their greatest collaboration" and helped us grow into our fullest selves. Knowing the challenges facing young women in physics, Dad went out of his way to fuel my passion. Once he drove me six hours to a lecture by a female physicist. His encouragement emboldened me to dive into a challenging field dominated by men.

Aissatou, on the other hand, has been taught that she should be dominated by men. When male visitors arrive at her house, the jubilant builder I know transforms into a meek and submissive servant, bowing as she acquiesces to their every request.

The difference? I won the lottery at birth: time, place and parents who gave me the chance to develop my passions. I am on a mission to give Aissatou and Binta the chance to do the same.

I think about the untapped potential of millions of girls like Aissatou and Binta, who lack opportunities because of custom, poverty, laws or terrorist threats. The gifted young women I've taught as a Peace Corps volunteer implementing the Let Girls Learn pro-

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be addressed. One is creating a diverse, inclusive and respectful environment. Another is really changing the power dynamics in adviser-trainee relationships. We need to make them less singular, to consider group mentoring, and to think about ways you might uncouple the mentoring relationship from financial dependence on the mentor. The third is supporting the targets of harassment, providing alternative ways to access services, whether or not they decide to report.

There are also certain structural aspects of the way we handle cases now that really work against what we're trying to achieve. For example, we made a recommendation that confidentiality agreements with perpetrators be prohibited. They prevent institutions from being transparent and inhibit them from being able to provide information that could be important to other institutions.

You also found that only a minority of people who experience harassment report it. How can we change that?

There are some novel approaches for reporting experiences of harassment that provide more control to the target. One is a program called Callisto that's now being adopted by a growing number of colleges and universities. It allows people to go in and record if an experience of harassment occurred and time-stamp it, without actually formally reporting it. People can see if others have recorded experiences with the same accused harasser. It allows people to share data in an anonymous way. It's a very hopeful, interesting tool.

Did the report address how harassment affects women of color and other minority groups differently?

We found women of color experience more harassment than do white women, white men and men of color. And that women of color also experience racial and ethnic harassment.

We crafted our recommendations with this finding in mind. Creating a more diverse, inclusive, respectful environment—that will help address this issue.

Your background is in medicine, which is the field within science where harassment is most prevalent. Why do you think that is?

The qualitative interview research commissioned by the committee provided some insight. It showed that with some of the expectations of grueling conditions in [medical] training, several respondents viewed sexual harassment as just part of the continuum of what they were expected to endure. Targets might say, "This is a really tough experience, and the conditions are pretty difficult, and [harassment] is part of that."

Are you optimistic that the changes you call for will take place?

I am. We all know that culture change is not easy and that it doesn't happen overnight. But neither did this problem arise overnight. We've seen leaders, myself included and many others, who are already taking the initiative to pursue some of the changes that we've suggested. Obviously, the fact that harassment is so prevalent is alarming. But we are providing a road map for a way forward, and I find that hopeful. And we're in a particular moment where I think we've got the will. SA

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gram have strengthened my conviction that it is possible for them to fulfill their promise through education. And educating girls is not only morally right but also provides a cornerstone of achieving a peaceful and prosperous future.

I wonder if Binta intended to leave me the clue to a brighter world in her quiz. After all, I reflected on moral metaphors in science when I was her age.

"What exciting thing did you learn today?" my dad would ask.

"We should all be like ideal gases," I responded one day after an exciting physics class. "They expand to fill whatever containers they occupy, so we can make the most of every situation too."

He smiled knowingly. "You know, gases with enough energy can even break open their containers."

When I see Aissatou squeal joyously on the improvised roller coaster she built from tree branches, I know that with the right support she could burst through her cultural container. If anyone has enough energy, she does.

Do you want to know something exciting I learned? Mass-energy equivalence means that the solar energy striking the earth each second equals only four pounds of mass. That means a small girl of 40 pounds could unleash the energy of 10 suns shining on the earth in a second. Take the 132 million girls who are not in school, and we have 1.32 billion suns in our daughters.

How will we help them rise? SA

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Illustration by Cat O'Neil

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Bringing Up Baby, Helping the Economy

Paid parental leave produces healthier children and businesses

By the Editors

Too often new parents feel terrified—and not just about the daunting prospect of raising a child. Many of them must grapple with a gut-wrenching decision: How quickly can they leave their newborn to get back to their job? Few can afford to go without salaries for long or to weaken their future wage-earning potential by leaving their job altogether.

Americans face such dilemmas because 88 percent of the private U.S. workforce is ineligible for paid family leave. As a result, many women and men clock back in to work within weeks. The cost of that decision can be measured in poorer health outcomes for their newborn and for themselves.

Right now the U.S. holds the dubious honor of being the only developed nation without policies guaranteeing parents a temporary paid leave from their job. Even countries with fewer resources offer better policies: in Costa Rica, for example, mothers receive full pay if they take leave during the final month of pregnancy and during the first three months postpartum.

Workers in the U.S., however, only get a chance at unpaid leave for three months after the birth of a child. And that narrow benefit, part of the 1993 Family and Medical Leave Act (FMLA), applies only to private companies with more than 50 employees (the unpaid offering also applies to public employees). Almost half of the U.S. population is ineligible. And because there are no federal paid-leave requirements, only about one in eight private-sector employees has a paid option.

That needs to change to improve our health and economy. Paid leave will keep families healthier. In countries with such policies, it has reduced infant mortality by as much as 10 percent. It also helps to improve new parents' emotional well-being. And multiple studies indicate that paid maternity leave is associated with increased rate and duration of breastfeeding. That practice, pediatricians agree, promotes better health for a newborn.

Paid leave need not come at the expense of profits, either. During the 2016 presidential campaign, Donald Trump cited concerns about businesses' bottom line for his reluctance to embrace the paid approach (although ultimately he did propose a six-week paid-leave plan). There is already good evidence that paid leave would not hurt businesses. The experience of a few states that have enacted paid-leave laws shows they produce good results for employers and employees alike. States such as California, Rhode Island and New Jersey have mandatory paid-leave requirements, ranging from four to six weeks at partial pay. The money comes entirely from employee payroll deductions—not out of employers' pockets. In studies of those states, most businesses subsequently reported that such policies had no negative effect on their profitability or productivity, and employers said employee morale improved. Private companies in the U.S., including Microsoft, Goldman Sachs, Nestlé and Facebook, think it makes good economic sense, too. They say they voluntarily offer their employees paid family leave to increase workplace competitiveness and employee retention.

Scattered state and company support for paid leave, however, is not enough. A national policy would enable employees and companies throughout the country to share in these documented advantages. It would also help eradicate other workforce inequities, including long-standing gender pay gaps that are exacerbated when women exit their job to tend to children. (Paid leave allows women to remain in the workforce, reducing holes in a résumé, which helps to address the differences.) If more people are working, that may also reduce government spending on public assistance.

Such policies also promote shared responsibilities in the household. One study of working fathers in the U.S. found that new fathers who took leave of two weeks or more were much more likely to be involved in their child's care nine months after birth—including feeding, changing diapers and getting up during the night when their child needed a parent.

It is time to take federal action and secure at least a month of paid family leave before ultimately scaling up to several months of paid support. Without paid family leave, we are all paying too steep a price. SA

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